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What Mr Blix should do

UN's atomic energy agency has been through a bad patch. Its new director should resurrect its original purpose.

The International Atomic Energy Agency in Vienna has plainly been scarred by the events of the past year, the Israeli raids on the Iraqi reactor at Tamuz among them. But for most of the year the agency has also been haunted by the unaccustomed difficulty of deciding who should be its new director general. Dr Sigvard Eklund, who until September had held the post for eight years, had not simplified the transition by making no secret of his willingness to serve for a third term: but the agency's governors were also perplexed in choosing between the two candidates on offer — Mr Hans Blix, deputy foreign minister of Sweden and Mr Domingo Siazon of the Philippines. The difficulty has been largely that of choosing between candidates from developed and developing countries. Exactly the same problem has more recently cropped up in the United Nations itself. The upshot of six months' heart-searching in Vienna is that Mr Blix has now taken up the post of director general. But he will probably be challenged again when his term expires four years from now. The danger is that the agency, hitherto almost as free from politics as the World Meteorological Organization, will fall foul of the squabbling to which most other United Nations organizations are prone. Mr Blix should therefore bend his energies to the insulation of the agency from the petty endemic politics of the United Nations system.

How is this to be accomplished? A sense of history will help. The Vienna agency is the product of President Eisenhower's programme in the 1950s that rejoiced in the slogan "Atoms for peace". Nobody doubted, then, that nuclear power stations would spring up apace in the territories of the nuclear powers, bringing prosperity in their wake: what more natural, even at the height of the Cold War, than that the United States and the Soviet Union should offer to share the benefits of their new technology with less fortunate governments? Even in the 1950s, however, people had forgotten that the agency they created had only its name in common with the much grander concept put forward in 1947, as part of the Baruch plan, of a United Nations agency that would literally be the sole owner and custodian of fissile material. The agency that Mr Blix has inherited is best known as the entity responsible for the administration of the safeguards required of non-nuclear power signatories of the Non-Proliferation Treaty: programmes of technical assistance continue, but on such a modest scale that they can make very little difference to the expectations of non-nuclear states that they will be able to decide for themselves even such simple questions as whether the much disputed benefits of nuclear power apply to them. The unaccustomed quarrelsomeness that has now emerged among the 111 member states at Vienna owes something to the belief that the agency should be doing more to spread such benefits of nuclear power as there are. The discontent is entirely justifiable.

The agency's most urgent need is for a realistic programme for helping developing countries to make sober appraisals of the utility of nuclear reactors. There is a limit to the extent to which they can be fobbed off with technical advice from international consultants on the place of nuclear technology in, say, agriculture. But where, the agency will ask, are the funds with which to support a more ambitious programme? For the time being, the unwillingness of the chief members of the agency to contribute more towards its budget is not its chief impediment.

At frequent intervals in the past two decades, the agency has published assessments of the place of nuclear reactors in the

economies of developing countries whose optimism has been matched only by their naivety — and which have nevertheless contributed to the present sense that the major nuclear powers are malevolently keeping nuclear power to themselves. Mr Blix should begin by commissioning a more realistic (and more technical) appraisal of the place of nuclear power in the smaller member states of the agency. He should then go further, for the assessment would almost certainly conclude that, within a decade, a great many smaller states will be able to make good use of the occasional well-sited and well-designed power reactor; he should offer a technical appraisal service for developing countries unable to decide between the claims of rival reactor salesmen.

Naturally, many of the founder members of the agency will object to such proposals. Appraisals that are too realistic may persuade some customers that the time has not yet come when they should buy. In the long run, however, that can only benefit the reputation of nuclear power and thus of its application. Others will protest that the encouragement of nuclear power can only assist the proliferation of nuclear weapons. The reply is two-edged. First, the involvement of the agency in the provision of civil nuclear power is likely to ensure that the safeguards procedures are effective. Second, the Non-Proliferation Treaty is a bargain in which non-nuclear powers agree to forsake nuclear weapons in return for a promise by the nuclear powers that they will assist with civil development. There is no way in which the nuclear powers can escape the commitment except by abrogating the treaty. Their best course is to help ensure that the safeguards procedures are continually improved.

To this end, Mr Blix could usefully consider whether the agency should soldier on as an amalgam of an international regulatory agency and a technical assistance organization. There is a strong case for reconstituting the safeguards organization as an independent quasi-judicial entity, perhaps a kind of permanent secretariat of the Non-Proliferation Treaty. Four years from now there will be a review of the working of the treaty. If safeguards are to be reorganized by then, it is not too soon to start. Fortunately, the wind is blowing in the right direction. The United States Administration is ready to loosen its restrictions on the export of reactors, but would find it convenient if the safeguards procedures were at the same time made more explicit. The agency's committee on the security of supply of nuclear materials, set up after the abortive conference in 1980 on the working of the Non-Proliferation Treaty, needs something tangible in which to sink its teeth. And with Mr Blix being a newcomer there is an ideal opportunity for change.

Congress versus cancer

The US Congress would legislate against cancer. It must be patient.

Part of the strength of democratically elected bodies, the United States Congress included, is that they are not necessarily bound by the decisions or the prejudices of their predecessors. That, however, is not a sufficient explanation of the way in which the present United States Congress, still less than a year old, seems bent on repudiating its predecessors' fondness for those agencies in the front line of what many congressmen used to call the "war



against cancer". Yet it is less than ten years since President Richard M. Nixon and Senator Edward M. Kennedy were vying with each other to devise still more generous programmes for cancer research. Over the years, the National Cancer Institute, a constituent of the National Institutes of Health, has been the centre of most of this attention, with the result that its operating budget now exceeds \$1,000 million a year. But something has gone wrong. Now hardly a week seems to pass without the director of the institute, Dr Vincent T. DeVita, appearing before one investigative committee or another to defend his institution against some fresh set of allegations. What can be the explanation? Has Congress fallen out of love with the war against cancer, or is there a more sinister explanation?

Part of the trouble is that Dr DeVita is new to the job — he took up his post only at the beginning of the year — and better known as a scientist than as a politician. Indeed, it seems that he has concentrated in the past few months on bringing a sense of direction to the research programme that he is paid to direct. This part of his job seems to have been done with such flair that when, earlier this year, Senator Hatch's committee sought to saddle him with responsibility for the earlier maladministration of research grants, a group of Dr DeVita's colleagues wrote expressing their admiration for their new director. Nobody would be surprised, however, if in the course of spending more than \$20 million a week on research, Dr DeVita has neglected to pay court as assiduously as he might to those who hold the purse strings in Congress. Or is it that Congress, like the National Institutes of Health, is waiting to see if the new director will turn out to be a political appointment, the Administration's representative within the institutes and not the institutes' means of interceding both with the Administration and with Congress? It goes without saying that a political appointment, a sharp break with precedent, could be disastrous for the National Institutes of Health, whose most urgent collective need is coherence and not further partition.

Dr DeVita's problems are nevertheless substantial. Accusations earlier in the year that some research grants had been used and administered in such a way that data of doubtful value had been gathered appear to have been substantiated. Neither then nor since, however, has Congress asked itself whether such incidents, acknowledged to be rare, can be avoided in such a gigantic programme for throwing money at the problem of cancer. Much of the same is true of last week's hearing in the House of Representatives, when Dr DeVita was required to deal with newspaper allegations that cancer patients treated with novel drugs within the framework of agreed experimental protocols had died as a result of the drugs rather than of the diseases the drugs might, with luck, have treated. How else, it might be asked, can novel drugs be tried in human beings? This week, Senator Paula Hawkins will return to the same charge; she has been asking, ever since she reached the Senate in January, why, a decade after the war against cancer was conceived of, people still die of all but a few forms of the disease. It is to be hoped that Dr DeVita and his colleagues will have the courage to tell Senator Hawkins the truth. The war against cancer was misconceived. The idea that such a problem might be made to go away by spending money was always destined to end in disillusion. From the start, it has been plain that while even successful methods of treatment lack a sufficient basis of understanding, they cannot be generalized. Yet, it must also be made clear, developments in the past few years promise substantial steps in the right direction, whatever that may be.

The practical consequences of such a confession on the part of the National Cancer Institute need not be as disastrous as they might seem. Congress may (separately from this week's proceedings) reduce the budget earmarked for the institute. It may have no choice. But the cancer institute would be more easily managed, and would be more effective, if it were forced to be more discriminating, at its very generous margin, in how its funds are spent. And the enterprise that it represents would be much less vulnerable than at present to the constant sniping that now afflicts it if both Congress and the United States public understood more clearly that they must be patient.

Shame on New York

*Baseball has become a game of chance.
How should it be reformed?*

The city of New York has had a bad week. The leading article in last Thursday's *New York Times* was understandably entitled "The shape of New York's shame". Oddly, however, the newspaper was castigating the city council for a piece of flagrant but routine gerrymandering with the city's electoral boundaries, incurring as a result a reproof from the courts. But last Thursday morning, the shame hanging over the city was the humiliating defeat the previous evening of the city's most prosperous baseball team, the New York Yankees. In the process, the Yankees also lost the best-of-seven competition between North American baseball teams quaintly known as the "World Series". Last week's defeat was all the more galling because the Yankees were soundly beaten by the Los Angeles Dodgers, within living memory resident in Brooklyn and much resented for their defection. This gloom is yet another proof that something must be done to reform spectator sports in which the object is to hit a ball with some solid object, in baseball called a "bat".

At least to a first approximation, the interaction of a baseball and a bat is a soluble two-body problem. The bat in baseball is a simple object, cylindrically symmetrical about an axis, while the complication arising because some ball-throwers (called "pitchers") claim to be able to throw "curve-balls" is irrelevant to last week's disasters because both teams appear to have been incapable of hitting them. Moreover, since baseball officials have taken to measuring the speed with which individual baseballs are delivered, there is a wealth of empirical data on which a proper mechanics of baseball might be founded. Speeds of up to 40 metres per second are recorded.

The difficulty of baseball is, first, that of hitting the ball and, second, that of knowing where it will go when hit: good players appear to be able to hit one fair ball in three, but usually even the best players appear at a loss to know whether the ball will shoot high in the air (in which case it may be caught and they will be dismissed), vertically downwards into the ground or upwards and backwards, into the crowd. Only occasionally, perhaps half a dozen times in several hours, does the ball perform as every batter hopes, carrying over the boundary fence for a home run. Thus, it appears, baseball has become an elaborate game of chance. In this year's World Series, there seems to have been very little to choose between the batting performance of the two teams. Part of the reason why the Yankees lost is that they were not as skilled at catching and throwing the ball as were the Dodgers. It is now a matter of great importance to devise some way of ridding baseball of the luck on which it now depends, and which is a simple consequence of the circular cross-section of the baseball bat. Is there a place in baseball for the cricket bat?

Even New Yorkers will, however, agree that the most serious cause of the Yankees' defeat was the evil chance that attended one of the crucial decisions by the team's manager, Mr Robert Lemon. The issue is complicated by the requirements of this year's rules for the World Series that the pitcher, the man who throws the ball for his team, should also take his turn with the bat. At a point half-way through last Wednesday's game, Mr Lemon exercised his right to replace his successful pitcher due to bat with somebody reputed to be more skilled at hitting the ball, but who promptly failed to do so. Yet if the gamble had succeeded, the Yankees would have gained three runs and the Dodgers would have been too demoralized to sustain the struggle. What will happen now to Mr Lemon, who works for an owner so hot-tempered that he had to watch Wednesday's game with his hand in a cast after a fist-fight in a Los Angeles elevator, remains to be seen. Wisely, he has been keeping his own counsel. But is it not demeaning, and intolerable, that grown men's careers and the temper of a great city should be determined by the apparently random trajectories produced by trying to hit a baseball with a cylindrically symmetrical bat?

Back to basics for high-energy physics

US panel's ritual defence of accelerator

Washington

The high-energy physics community in the United States is lifting only the littlest of fingers in defence of the proton-antiproton accelerator ISABELLE at the Brookhaven National Laboratory, Long Island. At a day-long meeting on Sunday, the influential High Energy Physics Advisory Committee accepted a subcommittee's recommendation that the accelerator should be completed only if there were a prior assurance of adequate support for research at the two other accelerator laboratories at Stanford, California, and Fermi National Accelerator Laboratory (Fermilab), Illinois.

ISABELLE may thus turn out to be the most conspicuous casualty of the new financial restraint. The physical infrastructure of the machine, a tunnel 2.5 miles in circumference, is 95 per cent complete. But something like a further \$500 million would have to be spent on magnets, vacuum systems and radio-frequency accelerating cavities if the accelerator was to be finished by 1990.

If the project is abandoned, some 400 technical people at the Brookhaven Laboratory will be without jobs. There is even the gloomy possibility that, without its chief task, the survival of the laboratory itself will be in jeopardy.

The subcommittee report, the sole item on Sunday's agenda, had been prepared in less than three months by a group under Dr George Trilling of the University of California, Berkeley. The panel will go on to produce a more measured statement in January of the benefits that may derive from particle accelerators based on novel principles such as those being developed at Stanford and Cornell universities. This week's interim report was made necessary by the Department of Energy's need of an opinion from the high-energy physics community in advance of this week's crucial decisions within the Administration on how the latest 12 per cent budget cuts will be distributed.

Given the conflicting interests of its members, the panel's chief conclusion is understandably delphic. It "strongly recommends" that ISABELLE should be completed, goes on to argue that the total cost of high-energy physics to the Department of Energy would then be \$440 million a year and remarks that if this support is not forthcoming, the ISABELLE project cannot be continued.

At present, high-energy physics is

operating on a budget of \$325 million a year, at which level the principal accelerators cannot be operated full time for lack of funds with which to pay the electricity bills.

There is every sign that high-energy physics has reached a turning point in the United States. Three distinguishable constituencies have emerged — the operators of the accelerators at Fermilab and Stanford, who wish to see their equipment fully used, the adherents of ISABELLE, who argue that it is an essential tool for the 1990s, and the general university users of accelerators, who need more immediate access to existing machines but who recognize that without ISABELLE they will have even fewer experimental opportunities ten years from now. The interim report spells out the conditions that must be satisfied before funds are spent on the completion of ISABELLE:

- Full utilization of existing accelerators.
- Completion of the Tevatron I accelerator upgrade for colliding 1,000 GeV protons and antiprotons based on existing Fermilab accelerators.
- A start on work on the Tevatron II

project, intended as the chief fixed-target accelerator for the 1980s.

- Development of superconducting radio-frequency cavities (at Cornell University).

- Development of novel accelerator designs.

Much of Sunday's meeting was occupied with the cost of this minimal programme, eventually fixed at \$395 million a year: if ISABELLE were to be completed, the total high-energy physics budget of \$440 million a year would include an average of \$80 million a year for the construction of the machine. If, however, ISABELLE is abandoned, the committee argued, it would be necessary to spend an extra \$35 million on research and development on new accelerator technology.

The committee's optimism that its "minimal" programme may be funded derives from the agreement in 1979 between the Department of Energy and the Office of Management and Budget that high-energy physics could count on a budget of \$300 million a year, adjusted for inflation. Several members argued that even with the completion of ISABELLE,

Top men resign in CNRS crisis

The two heads of the largest research agency in France — the Centre National de la Recherche Scientifique (CNRS) — fell last week in a self-delivered *coup de grace*.

On Wednesday, M. Jacques Ducuing, the director-general of CNRS, handed in his resignation to the minister for research and technology, M. Jean-Pierre Chevènement. Shortly after, the president of CNRS, Professor Charles Thibault — who worked in tandem with Ducuing — resigned also. He was followed by three of the six scientific members of the CNRS council, and the other three, including Louis Néel, a Nobel laureate representing the Académie de France, are likely to resign soon. (Néel, however, awaits the recommendation of the Académie.)

So what was the fuss? Chevènement was planning to wait until early next year before making any major changes at CNRS (and elsewhere) by which time he would have tested the water with the national colloquium on science and technology. The unions were unhappy with the CNRS directorate and had called for their resignation; but there was no sign of any movement yet.

Then, on Tuesday, after a long Socialist Party congress in which the party appeared to move to the left and chided the government for failing to confront the establishment more firmly, Chevènement decided he wanted to sack M. Christian Morisson who was appointed director of social sciences at CNRS in April (before the general election).

Morisson, it seems, was taking CNRS

social science in completely the opposite direction from Chevènement's own interests. The minister would like to expand social sciences in France, but in the direction of immediate public concern — such as unemployment, or the changes implied by new technologies. Morisson's interests were more academic.

So Chevènement called Ducuing and asked him if at the council meeting due the following day he would propose that Morisson be replaced by someone more sympathetic — a M. Maurice Godelier, professor of anthropology at the Ecole des Hautes Etudes. Ducuing asked for more time to consult his colleagues but was refused. He resigned, and the other resignations followed, on the principle that the minister's insistence was an interference with scientists' responsibilities.

Chevènement, however, did not seem too disturbed by the events, despite the cries of some that the resignations would throw out of joint his whole plan for the reorganization of science and technology in France. At a press conference on Wednesday he asked journalists why they were so excited about the affair, pointing out that he had only proposed one change whereas in America the whole top administration was turned over at a change of government.

The minister now has a clear field on which to place his men, well before he had expected the opportunity. He is likely to be quick to make new appointments, though they must be approved by the council of ministers.

Robert Walgate

their budget is in real terms not very different from what was agreed three years ago. Others say that little purpose is served in reminding one Administration of promises made by its predecessor.

One of the ironies of ISABELLE is that the problems of magnet design which have delayed the project by about four years appear in the past few weeks to have been resolved. If the Administration practises what it has been preaching the only remaining hope for the accelerators is that Congress may choose to appropriate funds for the project against the Administration's wishes.

High-energy physics

LEP approved

While American physicists agonize over the future of a new accelerator (see above), twelve European nations last week agreed in principle to the construction of LEP, a 27-km circumference machine to collide electrons with positrons at energies up to 50 GeV per beam — enough to create the long-sought neutral intermediate vector boson.

The twelve nations are the members of CERN, the European centre for research on nuclear physics at Geneva where LEP will be constructed. Three members (the Netherlands, Sweden and Norway) have given approval subject to parliamentary approval at home.

The principal questions still hanging over LEP concern the precise annual budget at which it will be built — which affects how rapidly it might be brought into service — and environmental opposition in the French and Swiss territory under which the LEP tunnel must be bored.

If all goes well the budget will be decided at the December meeting of CERN Council. (On CERN's own plans, it would be about 630 million Swiss francs a year — £182 million — enough to have LEP in action by early 1987.)

But environmental approval is more unpredictable. At present, CERN is restricted from building even a reconnaissance gallery. The gallery is needed to permit inspection of the geologically critical boundary between the sandstone floor of the Geneva valley and the limestone Jura Mountains to the north (under which the LEP tunnel must pass), but a Lyons court ruled that CERN had no valid licence for the work. CERN has now guaranteed that the accelerator will not be built until and unless the appropriate local French and Swiss procedures for approving large constructions are completed successfully.

Such approval is yet to come — for the French and Swiss accession to LEP at the level of CERN Council was made at ministry level, and is subject to local approval. However, CERN staff are confident that the environmental "dangers" of LEP — for example that it might affect the water table — have been wildly exaggerated, and that local approval will be granted.

Robert Walgate

US research support

Academy exhales

Washington

Dr Frank Press's first essay as a constituency lobbyist since his election as president of the National Academy of Sciences, his colloquium on the latest budget proposals on Monday and Tuesday last week, was a tactical success. Its most tangible product, a document labelled "consensus statement", drafted in a closed session on the second day, is a nice amalgam of moderate belligerence and sympathy for the Administration's economic problems.

The colloquium itself was the first response of what the labour unions might call organized science to the decision in September that all federal agencies except the Department of Defense must reduce their discretionary expenditure by 12 per cent. (NASA, for the current financial year, is let off lightly at 6 per cent but has been told that 1983 will be worse). Discretionary expenditure is that not mandated by explicit provisions in legislation.

The consensus statement acknowledges that economic problems "have eroded research and development", but says that the new budget proposals will do "irreparable damage" unless long-term research is protected, if necessary at the expense of "development and demonstration". The document urges the Administration to assume responsibility for supporting scientific research, but asks for a formal review of the machinery by which this is done.

Before the definition of consensus preoccupied the colloquium, diversity was rampant. One speaker was so alarmed by the threatened 12 per cent reduction as to fear a return to pre-Sputnik days. Another warned his academic colleagues not to expect too much from industry, whose support now accounts for 3 per cent of university budgets. Industrial grants would have to increase threefold to make good the damage done by the 12 per cent cut.

The colloquium also broke new ground by giving currency to the word "prioritization" — deciding what research should be given first claim on limited funds. This notion is in sharp contrast with earlier declarations of faith in a plurality of sources of funds.

The statement argues that the abruptness of the new cuts will be especially damaging. This is well illustrated by the plight of the National Science Foundation, none of whose expenditure is mandated by Congress, but which finds itself committed to the US Navy for support of the Antarctic research programme as well as to several national laboratories. It has become known in the past few days that these commitments may mean that the softer, grant-making parts of the foundation may find their budgets cut by up to 18 per cent, especially if spending on social science,

education and international relations (cut severely in March) is now protected.

Among the hundred participants the two principal government representatives appear to have left contrasting impressions on their audience. Dr J. Khaduri, one of the hard men from the Office of Management and Budget, preached economic realism and told his listeners that they would lose more from continued inflation



Press, moderately belligerent; Keyworth, inscrutable

than from the government's emergency budget. In the meantime, he declared, there is bound to be hardship. But at least there is also a chance that scientific enterprise could be growing again on the basis of a "new equilibrium" and with the help of dollars whose value remained constant from one year to the next. It is unfortunate that the Secretary of the Treasury, Mr Donald Regan, should have had to admit a few days later that the federal budget would probably not be balanced by 1984.

Dr George Keyworth's declaration seems to have been harder to interpret. The science community is not yet sure whether to regard him as a friend at court or as the Administration's lightning rod. Dr Keyworth himself is probably not yet sure. Last week, however, he left at least some of his audience with the impression that he believes the consequences of the emergency budget will be less serious than now seems likely. Does he know something, or is he simply being well mannered?

European space policy

New satellites due

Europe's activities in space received new impetus with the announcement last week that the United Kingdom is willing to make its contribution to the Large Telecommunications Satellite (LSAT-1), and with the decisions made at a European Space Agency (ESA) council meeting to recommend three projects to member nations for further development. Provided the member states do not refuse to fund them, the three projects — the Earth Resources Satellite (ERS-1), the Ariane 4 launcher and the Spacelab "follow-on" spacecraft — will begin their next development stages in about three months' time. Other issues of great concern to the members of ESA — particularly collaboration with the United States and the ten-year plan of ESA's director, Erik Quistgaard (*Nature* 290, p.536) — have

been deferred until the next council meeting in December.

The Minister for Information Technology at the British Department of Industry, Mr Kenneth Baker, announced last Friday that the United Kingdom was willing to provide its 34 per cent share towards the cost of LSAT-1 (which would amount to about £77 million over the next ten years). The project will only proceed once other interested ESA members, particularly Italy, the Netherlands and Canada, have decided to fund it.

The concern of the United Kingdom has been that the balance of responsibilities for the specifications, management and marketing of the satellite, both before and after its expected launch on Ariane early in 1986, should be shifted from ESA to industry. The satellite will carry four groups of payloads, two of them primarily commercial, the others more experimental. The former are to be funded mainly by Britain and Italy, and are intended to provide efficient communications for businesses and facilities for high-powered direct broadcasting of television. The two more experimental payloads, involving Italy and Belgium, will function in the millimetre (20–30 GHz) waveband, and are intended to investigate signal propagation characteristics at these frequencies. Once the usefulness of LSAT-1 has been adequately demonstrated, further satellites of this type may be developed on a commercial basis and — to this end — the satellite has been designed to be launched by either Ariane or the space shuttle.

The decisions made at last week's ESA council meeting have increased the chances for launches of the Earth Resources Satellite, Ariane 4 and the successor to Spacelab in 1986 or thereabouts.

The successor to Spacelab will involve the development of increased electrical power and mission duration within the present Spacelab configuration. ESA's recommendation, if funded by member countries, will initiate the construction of this craft. Moreover, there will begin a study into the development of a pallet that would be launched from the shuttle to be retrieved from low Earth orbit later.

Ariane 4 is, to some extent, ESA's answer to the space shuttle, in that current models of Ariane cannot launch the large payloads that may be required over the period 1985–95. Modifications to the first stage, allowing an increased fuel volume and the addition of liquid fuelled boosters, will increase Ariane's maximum payload capacity to 4,300 kg (as opposed to Ariane 3's limit of 2,460 kg). It is intended that Ariane 4 will not only launch single large satellites such as Intelsat 6 but also provide an improved dual launch facility.

The oceanographic remote sensing satellite ERS-1 is now set for the second stage of its feasibility study, involving a detailed design and costing. Experiments already earmarked for the satellite will investigate the wind field and ocean wave

heights. An announcement of opportunity has also been issued for prospective experimenters to fill the remaining 50 kg of payload capacity. The final decisions on the mission's design and instrumentation will be taken in 1983. One problem still to be decided upon concerns the distribution of data from ERS-1, particularly the degree to which this is centralized.

Philip Campbell

Environment research council Rothschild persists

The Rothschild customer/contractor principle, whereby British government departments (the customers) commission research in the research councils (the contractors) is still alive in environmental research, despite its demise in medical research and modification in agricultural research earlier this year. Its survival seems to be largely due to Sir Hermann Bondi, a well-known advocate of the principle, who has been chairman of the Natural Environment Research Council (NERC) for the past year.

Sir Hermann believes that the principle will work well, but only if NERC is careful to accept those contracts which will benefit its research as well as satisfying the customer. He also acknowledges the difficulties inherent in multi-customer contracts which can put a project at risk if one customer decides to withdraw support.

One such casualty is the £5 million Land Geological Survey of Great Britain which was threatened when the Department of the Environment, largest of the three customers, decided to cut its contribution for 1981–82 to two-thirds of its level in 1980–81 and to support only tactical research directed mainly at resource planning.

It plans a further cut in 1982–83. The result has been a substantial reduction in the amount of strategic and long-term research which is mainly geared to detailed geological mapping.

Despite these problems, however, Sir Hermann remains optimistic about the work of NERC. When introducing its annual report last week (HMSO, £4.00), he said that he had had a "marvellous time" during his first year as chairman. Although a slightly reduced budget has diminished the vigour with which the council can pursue some projects, he says he is impressed with the quality of the research it supports and sees no danger of stagnation.

During 1980–81, the year covered by the annual report, £26.1 million of the council's £72.9 million budget was earned from contracts, the remainder coming from the Department of Education and Science through the science vote. Support for universities, however, decreased slightly, with £75,000 less spent on new research grants than in the previous year (the council currently awards about £3 million of new research grants a year).

Judy Redfearn

Hoechst in Boston Contract cleared

Washington

Deft collaboration between the US General Accounting Office (GAO) and Congressman Albert Gore has now forced into the open the controversial agreement between Massachusetts General Hospital and Hoechst AG, the Frankfurt-based chemicals company. Earlier this year, representatives of the hospital declined to hand over their agreement with Hoechst to a congressional subcommittee of which Mr Gore is the chairman, on the grounds of commercial confidentiality. Under the agreement, Hoechst will support a new department of molecular biology at the hospital, spending more than \$50 million in the coming decade. In return, Hoechst will have the first refusal on an exclusive licence to exploit any patents generated by the laboratory during the period of its financial support.

The intervention of GAO, prompted by Congressman Gore, was based on the possibility of a conflict between the hospital's agreement with Hoechst and the requirements of the 1980 amendments of the patent legislation which, among other things, gave non-profit making institutions such as the hospital the right to first refusal of patent rights arising from federally supported research. The provisions of the new patent legislation came into force on 1 July this year, two months after the hospital's agreement with the company.

Evidently, the new agreement between Hoechst and the hospital has been drafted with the new legislation in mind. GAO says, in a letter to Mr Gore, that it should be possible for the hospital to keep separate the research funded by Hoechst and that funded by federal agencies, the National Institutes of Health (NIH) in particular. As things are, the hospital's research programme is supported to the tune of \$30 million a year by grants from NIH.

Difficulties will arise, according to GAO, only when there is doubt over whether a patent exploited by Hoechst has been supported exclusively by funds provided by the company, or where patents arising from jointly funded projects would be dealt with differently under the agreements between the hospital and Hoechst and NIH respectively. In all the circumstances, both the hospital and the company are likely to lean over backwards to avoid complications of this kind. Even so, when making public the terms of the contract on 16 October, Mr Gore uttered dark threats about the necessity that US institutions made strong with public funds should assist American and not foreign industry.

The details of the contract now published are unlikely to offend academic susceptibilities. Hoechst's support of the new molecular biology laboratory is defined by a programme of payments that will include the best part of \$18 million for

laboratory accommodation and equipment as well as \$50 million over ten years for running costs. Both sums are indexed against inflation, while the hospital administration will be allowed to charge an overhead percentage (within the \$50 million) equal to that agreed from time to time with NIH.

Under the agreement, the hospital is required to patent all inventions arising from sponsored work, but at Hoechst's expense. The company will be automatically entitled to an exclusive licence for exploitation, but the hospital will be able to take back the rights of exploitation if the company delays for more than three years: the agreement specifies that the director of the new department of molecular biology should be Dr Howard Goodman, who is already in post. One of the potentially contentious points in the agreement is that senior appointments be decided "after consultation with the company". The agreement also requires that those appointed should be "as appropriate" recommended for tenured appointments at Harvard Medical School.

On publication, the agreement requires that the company should be sent a copy of any proposed publication 30 days before

this is sent off for publication, during which period the company will decide whether patentable discoveries are involved: all those employed at the department will be required to sign service agreements declaring that the hospital authorities will be notified of any possibly patentable discoveries. Collaboration with others is permitted, provided that Hoechst's exclusive patent rights are not prejudiced. Consultancy for other companies and organizations is permitted so long as there is full disclosure and discussion with the director of the department.

The agreement also defines the way in which the proceeds from patent exploitation will be shared between the inventors, their department and the hospital at large. The agreement says that royalty percentages negotiated should ordinarily be half those appropriate to commercial agreements, and that royalty income should be deductible from the annual payments to which the company is committed.

The agreement now published is very similar to the outline account of it given to the Gore committee earlier in the year, so it is not obvious why the hospital withheld it from the committee.

SERC director looks to the future

Britain must collaborate with its European neighbours if it is to have a stake in building major new research facilities in the future, according to Professor John Kingman who succeeded Sir Geoffrey Allen as chairman of the Science and Engineering Research Council (SERC) on 1 October. Precisely how big and costly a facility will be before international collaboration becomes worth while will depend on SERC's future resources and on the needs of potential collaborators. But if SERC was embarking now on some of the major facilities it agreed in the mid-1970s then international collaboration would almost certainly make sense, according to Kingman.

Indeed, the council is already looking for European partners to help with the construction of the spallation neutron source at the Rutherford Laboratory which, at an estimated cost of £15 million, is due to come on line during 1984. One possible collaborator is Germany which has considered building a similar facility of its own. But the council has also held discussions with other countries which may wish to use the facility.

SERC's difficulties over building major facilities began in the late 1970s when its budget failed to keep up with inflation, forcing it to lengthen construction times for major facilities and leading to an inefficient use of resources. Worst affected has been the nuclear structure facility at the Daresbury Laboratory which was originally due to come on line in 1978. Technical difficulties and a shortage of money at the right time have delayed its commissioning

until March 1982, although the capital cost (£13.5 million at 1980 prices) has kept roughly in line with inflation. The synchrotron radiation facility also at Daresbury, which was commissioned last June eighteen months behind schedule, has suffered a similar, but less acute problem.

Despite a static budget, however, SERC has had some recent successes. Kingman is particularly impressed with the work of the council's three directorates in encouraging collaboration on engineering research between academics and industry. The council set up its fourth directorate in biotechnology last week (see this page) but Kingman is doubtful that it can afford to set up a fifth in microelectronics unless it can transfer responsibility for those in marine and polymer engineering to industry in general or the Department of Industry in particular.

One of Kingman's major problems will be how to maintain the quality of science in British universities which are suffering an unprecedented cutback in income. Although he is sceptical of government promises to maintain the real value of the science vote, he says that he is determined to maintain spending on research grants and studentships at least at its present level. That could mean convincing the Advisory Board for the Research Councils, which divides the science vote between the five research councils, that SERC should have a larger slice of the cake. It will also mean maintaining numbers in the face of overall cuts in research studentships already made by the Department of Education and Science.

Judy Redfearn

UK biotechnology

Still striving

The British Science and Engineering Research Council (SERC) last week launched a new directorate to foster collaboration in biotechnology between academics and industry and to forestall any brain drain of British biotechnologists to greener pastures abroad. The new biotechnology directorate is partly a response to a major study, chaired by Dr Alfred Spinks, which recommended nearly two years ago that Britain must act swiftly if it is not to lose out on the commercial development of biotechnology. Contrary to appearances, however, SERC has not been tardy in its response, according to Dr Geoffrey Potter, who will lead the new directorate. SERC's specialist panel on biotechnology spent the past year working out precisely what to do.

The biotechnology directorate will perform a function similar to the existing SERC directorates in polymer and marine engineering except that it will report to both the science board and the engineering board, reflecting the broad spectrum of research that biotechnology encompasses. One of its most difficult tasks, according to Dr Potter, will be to motivate process engineers, notoriously more reluctant than microbiologists to seize opportunities in biotechnology.

The directorate's funds will only be modest, £1 million this year rising to £2.4 million by 1984-85. The extra money will come from the Advisory Board for the Research Councils and from economies in SERC's other activities.

Most of the money will be spent on fostering collaboration through schemes already used by SERC to get industry involved in research in universities. These include the teaching company scheme and Cooperative Awards in Science and Engineering (CASE), both of which support postgraduate students on research projects relevant to collaborating companies, and the cooperative grant scheme whereby SERC and collaborating companies chip in to the cost of research projects in university laboratories.

SERC is particularly keen to encourage collaboration on fermentation, enzyme and immobilized cell technology, separation and concentration technology, product processing and recombinant DNA research. The directorate is to work closely with the Department of Industry which may take over funding of projects approaching the development stage, and with the Agricultural Research Council and Medical Research Council, both of which also support biotechnology.

One of the directorate's aims, according to Dr Potter, is to create sufficient jobs to dissuade British biotechnologists from taking posts in industry and universities abroad and even to persuade those who have already left to return. Dr Potter's concern about a possible brain drain is

shared by the members of a Royal Society working party, chaired by Professor W.D.P. Stewart, which will shortly publish a report on biotechnology and education.

The working party estimates that over the next ten years Britain will need 1,000 extra graduates and 4,000 technicians trained in biotechnology. It does not, however, favour new undergraduate courses specifically in biotechnology; training should instead be based on existing undergraduate courses in biology and chemical engineering followed by more specialized postgraduate courses.

The working party also supports a recommendation originally made in the Spinks report that the University Grants Committee should create 20 new lectureships in selected universities. That request, together with many of the Spinks recommendations, received short shrift from the government, which said in a White Paper earlier this year that the development of biotechnology in Britain should depend on market forces rather than government intervention.

Judy Redfearn

Hungarian protests

The use of psychiatric methods to treat political dissent has reappeared in Hungary for the first time in more than a decade, with the confinement in a Budapest mental hospital of Dr Tibor Pakh, a 57-year-old lawyer and activist from 1956. Dr Pakh's hospitalization evoked a sharp letter of protest from more than 50 Hungarian intellectuals and scholars.

Since the rise of Solidarity, Dr Pakh has issued a number of open letters supporting the Polish liberalization and censuring the Hungarian authorities for echoing Moscow's condemnations of it.

On 4 October 1981, Dr Pakh attempted to travel to Poland. He was stopped at the Hungarian frontier, his passport and personal papers were confiscated, and he was forced to return to Budapest. On 6 October, when his protest to the Procurator General's office failed to obtain satisfaction, he began a protest fast in the University Church in Budapest. Three days later, he was forcibly conveyed to hospital, and given intravenous feeding and heavy doses of psychotropic drugs including haloperidol, one of the drugs used in similar cases in the Soviet Union.

The group of intellectuals who signed the protest letter maintained a constant stream of visitors to the hospital, demanding to see Dr Pakh and also forwarded their protest to Solidarity, who published it in their uncensored bulletin *Niezalezność*. The protesters apparently made their point, and on 26 October, Dr Pakh was released, ostensibly on "readjustment leave".

Vera Rich

Interferon

Gamma winners

Molecular biologists at the Californian biotechnology company of Genentech have won the race to clone a sequence of DNA corresponding to γ interferon, the least understood member of the family of proteins which may yet find a place in the therapy of cancer and viral diseases. At the same time Molloy Laboratories, a subsidiary of Revlon, have been contracted by the US National Cancer Institute (NCI) to purify sufficient γ interferon from natural sources for initial clinical trials.

The Genentech results, briefly presented by Dr David Goeddel at the Second Annual International Congress for Interferon Research in San Francisco, not only establish the sequence of γ interferon but also show that bacteria, yeast or mammalian cells are able to produce γ interferon when supplied with the corresponding sequence of DNA.

The starting material for both Genentech and Molloy was human lymphocytes, prime producers of γ interferon. From them Genentech isolated a mixture of messenger RNA molecules, produced the complementary DNA molecules, and transplanted them into cells of the bacterium *Escherichia coli*. Bacteria were then isolated which were producing the antiviral activity of interferon but with the instability towards acid that distinguishes γ interferon from the α and β varieties. Finally the DNA responsible for that activity was sequenced and shown to be about the same length as that of α interferons but with an unrelated sequence.

Human lymphocytes are also the starting material for the γ interferon that Molloy, in return for \$270,000 from the NCI, are to produce by traditional methods of purification from normal white blood cells obtained as a by-product of blood transfusion. Their aim is to produce five billion units of γ interferon, enough for up to 1,000 human doses, by the end of September 1982.

It is a matter of speculation whether the Genentech and Molloy materials will be equivalent. A lot depends on whether there is a single γ interferon or whether, like α interferon, it is a family of related molecules. Genentech has no evidence of more than one species but if they do exist they are likely soon to be discovered either by the Genentech scientists or by those whom they beat to the first sequence, including Dr Charles Weissmann on behalf of Biogen, Dr Jan Vilcek of New York University Medical Center and Dr Leroy Hood of the Californian Institute of Technology.

The hope of all concerned is that γ interferon will be of greater value than its stablemates in the therapy of cancer. The hope stems from the fact that antitumour effects of interferon are thought to work through the immune system and that γ interferon is

produced by and has effects on cells of that system. Reasonably large clinical trials of α and β interferon against cancer and viral diseases are currently under way using material purified from cells. It will be some time before their value is clear and even longer before it is known if γ interferon is more effective.

Peter Newmark

Royal Botanical Gardens

Look to the margins

This week sees a new man in charge of the Royal Botanical Gardens at Kew in London — Professor Arthur Bell, a biochemist, formerly head of the department of plant sciences at King's College. And it could mean a very different approach for an institution with a 140-year history of traditional botany behind it.

The Royal Botanical Gardens today include Kew together with a 600-acre estate at Wakehurst Place in Sussex, and are run as a department of the Ministry of Agriculture, Fisheries and Food with a scientific staff of almost 500. The emphasis is still very much on the traditional pursuits



Bell in situ at Kew

of collecting wild plant species (Kew boasts the world's largest herbarium) and taxonomy. Kew's new director, however, brings with him an enthusiasm for plant breeding not seen there before. And Professor Bell has a clear goal in view — to change the pattern of agriculture in the Third World.

At present just thirty plant species provide eighty per cent of the world's food supply. Many of these basic food crops are now grown in arid conditions far removed from those in which their free-growing ancestors used to thrive. Professor Bell's contention is that there are many indigenous crops used only as animal fodder, or unpalatable because of the presence of toxins, which would give better yields than today's food crops if suitable variants were selected. Therefore much of Kew's effort will centre on isolating variants of these so-called "marginal" crops which do not produce toxins, but which still grow well in arid climates. In this way perhaps Kew will again become the important source of new crops that it once was.

Charles Wenz

CORRESPONDENCE

Brazilian funds

SIR — I would like to correct some of the statements made by Mr Bazin in his article "Brazilian research funds: Sliding backwards" (*Nature* 6 August, p.489).

First, the Brazilian government has a clear and explicit policy statement regarding science and technology. This was published in the form of the 3rd Basic Plan for Scientific and Technological Development (1980–85) and stated in the 3rd National Development Plan.

Second, the Brazilian government, in harmony with the high priority given to science, has maintained a steady and growing support for scientific and technological activities. Financial resources allocated to science and technology in the federal budget are shown in Table 1.

Table 1 Federal support for science and technology

Year	Science and technology budget (US\$ million)	% Of federal budget
1980	352	2.1%
1981	435	2.3%
1982	909*	3.6%

*Proposal now in discussion in Congress.

Third, the National Research Council (CNPq) which is the central coordinating agency for science and technology in Brazil, has had and has now an important role to maintain and reinforce this growing public

Table 2 CNPq's budget

Year	Total budget (US\$ million)	% Allocated for grants and scholarships
1980	122	31.9%
1981	144	33.7%
1982	188*	38.0%

*Proposal.

support for research in the country. The data in Table 2 show that CNPq's budget, as well as the resources allocated for grants and scholarships, have outpaced inflation.

ERNO IVAN PAULINYI

CNPq, Brasilia, Brazil

MAURICE BAZIN REPLIES — When considering whether Brazil's research spending has kept pace with inflation it should be remembered that inflation in Brazil was over 80 per cent in 1980 and is now around 110 per cent.

Gold standard

SIR — The reexamination of the gold standard in the United States is motivated by more serious concerns than your article on the subject suggested (*Nature* 24 September, p.246). For, despite its faults, the gold standard performed an essential function for which no other arrangement has so far been able to substitute in a democracy. It provided an impartial mechanism which the general public accepted as justification for the monetary discipline necessary to prevent accelerating inflation.

From 1717, when Sir Isaac Newton established the official buying and selling prices of gold at 77/9d and 77/10½d per troy ounce, until the outbreak of the First World

War in 1914 (apart from a period around the Napoleonic Wars), a pound sterling was worth ¼ ounce of gold (within 1 per cent), and it was universally accepted that the Bank of England should maintain adequate reserves of gold to guarantee sterling's convertibility. Thus, when official gold reserves fell below a prudent level, the steps necessary to increase them, including in particular the raising of interest rates, were accepted by the public (and the parliamentary opposition) in preference to the abandonment of the gold standard.

By contrast, since the last link with gold was broken in 1971, there has been no economic "yardstick" which is publicly accepted as an objective measure of sound monetary policy, and periods of economic difficulty are blamed on the incumbent government rather than on our own behaviour. Politicians have inevitably tried to "buy" popularity, and as a result, in only ten years, sterling has been devalued by 75 per cent in real terms, at terrible economic and social cost to the United Kingdom. The United States is surprisingly close behind.

There is, in fact, a very great need to link currency to a real measure of value in a system of which the soundness and impartiality are beyond question and clear to both public and politicians. However, the standard should not be some "short-lived exotic radioactive isotope" as you suggest, but should be a range of the durable, essential, basic commodities on which all economic activity depends. The many far-reaching advantages of such a policy have been described by a number of economists over the past century, but the specification of a practical system is complicated by the need for commodity prices to respond to market forces; they cannot be fixed as was the price of gold. Nevertheless it would be possible to achieve the desired results by establishing a rule by which official buying and selling prices of specified commodities were adjusted automatically according to the levels of official reserves. Such a system has been widely endorsed by economists from across the political spectrum, one writing in 1958: "It can be only a question of time before man's reason and self-interest overcome his inertia and these proposals are accepted. When they are they will define the beginning of an era as surely as did the introduction of the gold standard, but without its fatal weakness".

Institutional resistance to change has so far prevented the adoption of such an innovation. But until we do, inflation will continue, with all its destructive consequences (and economics will continue to be as unscientific as physics would be without the ruler).

P.Q. COLLINS

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Lab animals

SIR — Your article on "Protection for laboratory animals" (*Nature* 17 September, p.173) offers an ineffectual solution to the problem of how to regulate the use of animals in research. Your suggestion of establishing a committee at each institution empowered to sanction proposed uses of laboratory animals seems like an attempt to eliminate regulation entirely. No research facility would refuse to sanction the use of animals for an experiment in which funding has been previously granted.

For regulation to be effective, it must be done by the agency responsible for funding.

Ignoring humane and philosophical considerations, the need for regulation is generated by the sheer numbers of research facilities in existence today. In order to prevent wasteful duplication of experiments, a coordinating agency must be empowered to determine the usefulness of a particular project. Since public monies are usually involved, the usefulness and more importantly the uniqueness of a study must be determined. Of course, a certain amount of replication of experimental results is necessary, but as there is virtually no communication between facilities, a parent agency must be involved to keep track of who is doing what.

We have a responsibility to the animal community, from which we have gained much information at the expense of much suffering, to use individuals as prudently as possible. Whether or not you believe an animal is capable of suffering in human terms is not important. It is a living entity, entitled to the life it was designed to lead.

Regulation of the use of animals in research experiments is essential to assure the proper use of public funds as well as the compliance with laws governing the humane treatment of the subjects. A governmental body, specifically the agency responsible for funding of research projects, must be responsible for the regulations.

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SIR — I was pleased to see your editorial comment "Protection for laboratory animals?" (*Nature* 17 September, p.173). The Committee for the Reform of Animal Experimentation (CRAE), which is drawn from both houses of parliament and from the fields of science and medicine as well as animal welfare, has been seeking contact with members of the scientific community at all levels in order to find a "middle ground" where there can be agreement on many of the issues relating to the use of living animals for research. We would be very pleased to hear from those working with animals in laboratories if they have any points of view to express.

CRAE applauds your proposal for the setting up of ethical committees within research centres to act as a brake on undesirable experimentation. Such committees should be largely composed of researchers' peers but should also include what the courts describe as "the reasonable man", that is, responsible members of the local community.

The concept of ethical committees would fit very well with the Home Secretary's Advisory Committee proposals for a project licence as a requirement as well as a competence licence before a researcher could experiment.

One error in your editorial: although the 1876 Act requires experiments involving pain to be carried out under anaesthesia, such provision is the subject of exemption by the issue of Certificate "A" which permits the infliction of either severe or enduring pain, and it is only where an animal is found to be suffering severe and enduring pain that the experiment must be terminated.

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Committee for the Reform of Animal
Experimentation, Edinburgh, UK

NEWS AND VIEWS

Integration of foreign genes into the mammalian germ line: genetic engineering enters a new era

from Brigid Hogan and Jeffrey Williams

THE application of recombinant DNA technology to mammalian cells is gradually yielding a rich harvest of cloned chromosomal fragments containing specific genes and their flanking sequences. Some of these cloned DNAs have been reintroduced into tissue culture cells where in many cases they are efficiently expressed. However, these experiments are of little value when it comes to identifying DNA sequences which control the temporal and tissue-specific expression of genes during embryonic development. To study these problems, a number of laboratories have injected cloned DNA into early mouse embryos, and seen if the genes become stably integrated into the germ line.

It was hoped that the injected embryos would grow into adults, each carrying the same exogenous DNA inserted into different chromosomal sites in their eggs or sperm. Offspring of these individuals would then generate mouse substrains with the inserted DNA in all cells right from the start of development, allowing the effect on gene expression of such factors as neighbouring sequences, chromatin structure and DNA methylation to be assessed. The results of these experiments are now being reported in varying degrees of detail, and the consensus is that the bold approach has paid off, with the process of chromosomal integration being more efficient than people had dared imagine.

Support for the idea that cloned genomic DNA could be inserted into the germ line via the early embryo came from the work of Rudolf Jaenisch and his colleagues¹⁻³ on the stable integration of exogenous Moloney leukaemia virus (M-MuLV). When 4-16 cell or blastocyst stage mouse embryos are infected with virus and then implanted into foster mothers, around 10-40 per cent per cent of the adults show active virus production in various tissues. Of these animals, a high proportion of the males can be shown to have M-MuLV DNA integrated into their germ line, since on mating with normal females they produce male offspring which transmit M-MuLV to 50 per cent of the next

generation (only males are studied, to avoid problems of *in utero* transmission of virus). The original virus-producing males developing from infected embryos show only a variable and declining transmission of M-MuLV. There are at least two reasons for this. First, the virus may only infect a few of the embryonic cells, giving rise to an adult in which the tissues are a 'mosaic' of cells with or without integrated virus. Second, spermatogenic cells carrying M-MuLV may be selected against in the mosaic testis as the animal ages. However, the second generation M-MuLV positive males carry viral sequences in all somatic cells, and transmit the DNA as a normal, dominant, gene to 50 per cent of their offspring. Using the technique of embryo infection, Jaenisch has generated thirteen different mouse substrains (Mov 1-13) carrying M-MuLV in specific sites. Study of these substrains has led to the exciting observation that integration of virus into different sites results in different temporal and tissue-specific patterns of viral expression.

In Mov-1 mice, for example, virus production is first seen in the spleen soon after birth, while in Mov-13 mice virus activation occurs much earlier, in liver cells after only 16 days gestation. In other substrains, virus may never be activated during normal life. The pattern of M-MuLV expression is therefore influenced by the chromosomal site into which the virus is integrated.

The converse of this effect may be the influence of MuLV sequences on the expression of genes into or near which they are inserted. Recent studies from the Jackson Laboratory in Bar Harbor⁴ have shown that the *dilute* coat-colour mutation in DBA-mice is linked to an endogenous MuLV sequence, and that spontaneous revertants from *dilute* to wild-type (*d* to *d*⁺) have also lost the viral sequence. It is therefore possible that the original *d* mutation, as well as other coat-colour mutations, are the result of provirus

integration into the genome.

In the experiments of Jaenisch and his colleagues described above, infection of preimplantation embryos led to mosaic adults composed of cells either lacking integrated virus or with virus integrated into different sites. However, more recent experiments⁵ have shown that if MuLV DNA cloned from Mov-3 animals is injected into the cytoplasm of a fertilized egg, viral sequences can be found in all of the cells of the resulting adult. The integration does not appear to be direct, however, and is not into the Mov-3 site. Rather, it appears that the DNA is first transcribed and then reintegrated into a new stable site in the zygote genome. This method therefore provides a quicker way of studying the effect of chromosomal integration site on viral expression, and of inserting M-MuLV DNA into the germ line. Unfortunately, the answer to the problem of how to direct M-MuLV into a defined site remains elusive.

Laboratories attempting to insert functional chromosomal genes into the germ line have also tried injecting cloned DNA into the fertilized egg, although in these cases the DNA is actually injected into one of the two pronuclei before they have fused. The first reports to appear^{6,7} showed that recombinant bacterial plasmids injected in this way were retained in some of the surviving animals in a high molecular weight form. The amount of DNA present was sufficient to suggest that most, if not all, of the cells contained multiple copies of the plasmid. Two obvious questions arise. Has the foreign DNA been recombined into the chromosomes and, if so, does the germ line contain integrated DNA? Both of these questions are now elegantly answered in experiments published in this issue of *Nature* (see p.92) by Constantini and Lacey of the Department of Zoology, Oxford. They injected a λ recombinant containing the adult rabbit β -globin gene and a β -like pseudogene $\psi\beta 2$ in a 19 kilobase chromosomal DNA fragment. Partial hepatectomies were performed on 24 of the mice, and total liver DNA screened for the

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presence of rabbit β -globin genes by Southern blot hybridization. Nine of the mice contained rabbit β -globin genes in copy numbers varying in different individuals from one or two to up to twenty per cell although further experiments are now needed to establish whether the animals are mosaics, with some cells containing more copies and others none.

Four of the positive males were mated with normal females and DNA from the progeny screened for the presence of rabbit globin genes. Out of a total of eighteen progeny screened, six were found to contain rabbit globin sequences. This pattern of inheritance is consistent with a chromosomal location of the foreign DNA and, in a footnote to their paper, Constantini and Lacey describe the results of an *in situ* hybridization experiment showing that most, if not all, copies of the rabbit globin genes in one of their mice are located in the middle of one of the homologues of chromosome 1. The organization of the rabbit β -globin gene copies has been determined in a number of the mice by restriction mapping with various enzymes. Predominantly linear molecules of λ DNA were injected, but the integrated DNA contains the fusion fragment resulting from annealing of the λ cohesive ends. Consequently, the authors suggest that the input λ DNA is ligated to form high molecular weight concatemers and it is these tandem arrays which are then integrated into the chromosome. There is direct evidence that such a mechanism occurs for linear DNA injected into fertilized eggs of *Xenopus laevis*⁸. Also Constantini and Lacey detect minor fragments which are transmitted to progeny mice, and which probably contain the junction between the terminal copies of the foreign DNA oligomers and host chromosomal DNA sequences.

What then of the questions posed at the outset? Are foreign genes which have become stably integrated into the mouse genome expressed, and do they display the correct temporal and tissue specific pattern of gene expression? A newly published study by Wagner and his colleagues at Ohio University, describing work done in collaboration with Hoppe at the Jackson Laboratory suggests that at least the first of these two important goals has been achieved⁹. A proportion of mice, derived from eggs which have been injected with a rabbit β -globin gene were found to contain a rabbit globin polypeptide in their erythrocytes, and this was also true of their progeny. Furthermore, a recent report in *Science*¹⁰, quotes preliminary evidence

obtained by Wagner which indicates that the rabbit globin polypeptide was produced only in red blood cell precursors and not in other tissues of the mouse. If this latter observation is confirmed, the way would seem to be open to determining those features of DNA structure important in controlling gene expression during development. Also, of course, if it has indeed been possible to insert a cloned gene

sequence into the mammalian genome so that it functions correctly, the wider implications are enormous. Leaving aside the controversial question of gene therapy in humans, it seems certain that the genetic manipulation of agriculturally important animals will quickly follow, since, in cattle at least, the techniques of superovulation and reimplantation in foster mothers are now routine procedures. □

Extraterrestrials — where are they?

from Ben Zuckerman

IN THE MIDST of a sometimes depressing reality, many people take conscious or subconscious comfort in the assumption that we are but one of a myriad of advanced technical civilizations co-existing in our Milky Way galaxy. This view — championed by articulate scientific and lay spokesmen — is bolstered by lavish science fiction movies, by reports of UFO encounters of the first, second, and third kinds, and by best selling books about artefacts left behind by so-called ancient astronauts.

Included among the articulate scientific spokesmen is Carl Sagan of Cornell University, whose television programme and book *Cosmos* have brought astronomy into the homes of millions of Americans. Sagan, and some other well known scientists such as Philip Morrison (MIT) and Frank Drake (Cornell University), are considered to be members of the 'optimistic' school of thought on the question of extraterrestrial intelligence. They have argued that 100,000 or more technical civilizations, all of which have arisen independently, may currently exist in our Milky Way galaxy. If there are this many civilizations, then a typical one must exist for a million years or more.

How do the optimists arrive at this value for N , the number of technical civilizations in the Milky Way? Usually they rely on the 'Drake equation' which expresses N as a product of the various probabilities of the origin and evolution of life, intelligence, and technology. Sagan went through this exercise in *Cosmos*. He supplied his estimates for a long string of uncertain factors including, for example, the probability, $P(\text{life})$, that life will originate on an Earth-like planet and the probability that, having originated, it will then evolve to intelligence and technology. Since we really know very little about these probabilities, the optimists rely on the Copernican world view that we are not special. After all, most Europeans once believed that the Earth was located at the centre of the Solar System. After that was shown to be false, it was still commonly believed that the Sun was located at or near

the centre of the Universe. As this now also seems most unlikely, the optimists argue, so should be the view that intelligent life is unique to the Earth given that there are hundreds of billions of stars in the Milky Way and most of them have been shining for at least five billion years.

This world view compels them to choose very large values for the probabilities mentioned above. For example, many (most?) scientists would regard $P(\text{life})$ as uncertain by a factor of at least a million. Yet Sagan, in *Cosmos*, purports to know $P(\text{life})$ to two significant figures. His choice of $P(\text{life}) \sim 0.5$ is, ostensibly, the result of taking the *arithmetical* mean of unity, which he prefers, and zero which is preferred by some of the pessimists in this field. Of course, he would have obtained a very different value for N if he had instead set $P(\text{life})$ equal to zero, the *geometrical* mean of 1 and 0. This illustrates the kind of tricks that one can play with the Drake equation.

Until the past few years, there were very few scientists who would argue strongly against this Copernican philosophy. Ten years ago, when I first became seriously interested in this problem, I was sufficiently uncertain of the value of N that I attempted to search, with Patrick Palmer (University of Chicago), for radio signals from another civilization. We pointed the 300- and 140-foot telescopes of the US National Radio Astronomy Observatory towards approximately 670 nearby stars. Since then half a dozen similar attempts have been made by radio astronomers in the United States and Canada. None of these has been successful, unless someone is hiding something in their bottom drawer.

Radio beacons are, of course, but one of many ways that advanced technological societies could make their presence known to scientists here on Earth. The most obvious way would be for the extraterrestrials to send a manned or unmanned probe to our Solar System and, especially, to land one on Earth. That there is no real evidence that this has ever occurred has suggested to Michael Hart (Trinity University) and others that

1. Jaenisch *Proc. natn. Acad. Sci. U.S.A.* 73, 1260 (1976).
2. Jähner & Jaenisch *Nature* 287, 456 (1980).
3. Jaenisch *et al. Cell* 24, 519 (1981).
4. Jenkins, Copeland, Taylor & Lee *Nature* 293, 370 (1981).
5. Harbers, Jähner & Jaenisch *Nature* 293, 540 (1981).
6. Gordon *et al. Proc. natn. Acad. Sci. U.S.A.* 77, 7380 (1980).
7. Wagner *et al. Proc. natn. Acad. Sci. U.S.A.* 78, 5016 (1981).
8. Bendig *Nature* 292, 65 (1981).
9. Wagner *et al. Proc. natn. Acad. Sci. U.S.A.* 78, 6376 (1981).
10. Reported in *Research News, Science* 213, 1488 (1981).

advanced civilizations do not exist anywhere in our galaxy. We may well have the most advanced brains in the entire Milky Way.

At first glance it would seem to be a preposterous extrapolation to jump from the fact that we have not yet uncovered any evidence, either in deep space or in our Solar System, for superior extraterrestrial beings to the conclusion that they don't exist anywhere in the Milky Way. After all, our radio searches have been quite primitive and one can think of lots of reasons why another civilization might not want to go to the trouble and expense of sending complex probes between star systems.

This argument is reasonable if we are trying to understand why only a few civilizations might not want to send out interstellar spaceships. But what if there have been 100,000 or more civilizations, each of which must have existed, on the average, for a million years or more? Just as life and now, especially, intelligent life has transformed the face of the Earth so it might reasonably be expected that most of these 100,000 superior civilizations will have carried out deeds that, at present, we would regard as technological 'miracles'. Suggestions have included colonization and reengineering of the moons and planets of the home solar system to colonization and reengineering of the entire galaxy — all on time scales much less than 10 billion years.

Discussion of the many implications of these arguments filled an entire symposium whose proceedings, *Extraterrestrials — Where Are They?* are scheduled for publication by Pergamon Press in the autumn of 1981. Papers were presented by venerable pundits including, for example, Freeman Dyson (Institute for Advanced Study), Sebastian von Hoerner (National Radio Astronomy Observatory), and Ronald Bracewell (Stanford University) as well as by various comparative newcomers to this field.

Although many scientists find the arguments that *N* must be a very small number ($\sim$ unity) quite compelling, few, if any, believe them to be so compelling that we should abandon searches for radio or infrared radiation from extraterrestrial beings. It is, therefore, ironical that Senator William Proxmire (Wisconsin) has entered these arguments into the Congressional Record of 30 July 1981 as part of his justification for prohibiting the use of federal funds during fiscal year 1982 for a modest radio search programme under consideration by NASA's Ames Research Center and the Jet Propulsion Laboratory. (He also felt that NASA wanted to search in the wrong place: "I have always thought that if [our best scientists] were going to look for intelligence, they ought to start right here in Washington. It is hard enough to find intelligent life right here. It may even be harder, I might say, than finding it outside

our Solar System.")

A few years ago Proxmire succeeded in deleting federal funds earmarked for a similar NASA search programme and gave NASA one of his Golden Fleece awards. Frank Drake, in return, gave Proxmire honorary membership of the Flat Earth Society but all to no avail. NASA has attempted to keep the programme alive, albeit at a minimal level, by using discretionary funds but the recent congressional action has stopped even that, at least for 1982.

This decision seems unfortunate for two reasons. First, there is considerable public interest in the search for intelligent life, judging, for example, from the response to

Cosmos and the growing popularity of courses on "Life in the Universe" on college campuses. Second, and more generally, is it really in the best interests of American science for individual Congress-people to fiddle with relatively minor items (about a million dollars a year) in the much larger budgets of major institutions such as NASA? Or, in the absence of a congressional vote of 'no confidence' in the NASA leadership, shouldn't the latter group, in conjunction with their scientists and engineers, be the ones who determine expenditures at the megadollar level? □

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Histone gene organization: paradigm lost

from Larry Kedes and Rob Maxson

THE organizations of sea urchin and *Drosophila melanogaster* histone genes were shown, even before the era of gene splicing, to be remarkably similar: both are repeated in the hundreds and arranged in tandem units, each unit containing the intimately linked genes for five major histone proteins. While the differences between the sea urchin and the fruitfly histone gene topology hinted that the order and polarity of the genes within a species can be gently shuffled, the similarity between species so widely separated in evolutionary terms seemed to establish a paradigm for histone gene arrangement and lead to the confident expectation that similar arrangements would be found in intervening phyla.

However, a rash of recent reports of different patterns of histone gene organization in a number of different vertebrate species, including examples of scattered and often solitary genes, has dispatched classical notions about their fixed organization. The authors responsible for the new observations have been quick to point out the difference between the more familiar sea urchin-fruitfly tandem organization and the vertebrate dispersed topology and to speculate on its significance. Human¹⁻³, mouse⁴, chicken^{5,6} (see this issue of *Nature*, p.49) and toad⁷⁻⁹ genes have now been cloned. Not only are the genes differently arranged in comparison with the classical paradigm, but they seem scattered and separated by long stretches of non-histone DNA (for an extensive review see ref 10). While a few coding regions remain clustered, they are not at all arranged in clean-cut tandem repeats. Some coding regions are solitary and separated, by at least 10 to 20 kilobases, from their fellows. None seem to be an

identical copy of any other suggesting that dispersion allows, or at least associates with, evolutionary drift in gene sequence. Each coding region seems to be present only in tens per haploid genome. How close the histone gene members of this newly discovered diaspora are to one another in the genomic landscape has yet to be determined. An earlier report¹¹, using *in situ* hybridization, suggests that the human genes may be landmen: the locus seemed confined to the telomere of chromosome 7 but the genes are scattered over the entire distal third of the long arm.

Recent findings in our own laboratory suggest that the distinction between clustered and dispersed histone gene organization is not a strict interspecies difference. As pointed out by a number of workers, a gradual shift in expression occurs during early sea urchin development: the activity of the several hundred-fold tandem clustered 'early' gene set is reduced in favour of the expression of a set of 'late' histone genes of much lower copy number. Some features of late sea urchin histone gene organization have now come to light with the cloning of several examples¹². The late genes are scattered and shuffled not unlike those described for the vertebrate examples mentioned above. Genes coding for isoforms of the same histone exhibit extensive nucleotide sequence divergence. And to complicate matters, not all of the vertebrate genes follow the same model: histone genes in the newt¹², *Notophthalmus viridescens*, share all the topological features of the sea urchin and fruitfly clustered arrangement except that each repeat unit is separated by a long

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stretch of satellite DNA.

Evolutionary models for the establishment of tandem gene clusters either from dispersed gene duplications, or by dispersal of gene elements from a tandemly amplified gene family, seem to be equally possible. Isolated dispersed members of tandem gene families¹⁴ have definitely been found among sea urchin and *Drosophila* histone gene families and among mouse alpha-globin genes¹⁵. Thus, mechanisms do exist that allow copies of gene regions to be banished to remote corners of the chromosomal countryside where they can diverge and possibly take on a new function or fall prey to new regulatory controls. Such a scenario may represent the mechanism that generated dispersed late sea urchin histone genes from the repetitive early cluster. Catastrophic deletion of an amplified cluster following speciation could account for the absence of tandemly repetitive histone genes among most vertebrates.

Equally convincing evidence may exist on the side of an explanation that holds that scattered organization predates the amplified cluster of genes. The yeast, *Saccharomyces cerevisiae*, has H3 and H4 genes head to head at one locus and H2B and H2A lying at another locus in the same posture¹⁶⁻¹⁸. Both loci are duplicated so only a dispersed organization exists in this protistan. Simple amplification by gene duplication and unequal crossing-over within one of the scattered clusters of histone genes may be the organizing principle that might generate a tandem cluster. There are those who correctly point out, however, that yeast is a simplified evolutionary descendant of more complex protista and that an examination of histone gene organization in algae or slime moulds, for example, might better establish the validity of this model.

These observations about apparently chaotic principles underlying the alternative arrangements of histone genes can hardly be considered as a "paradigm regained" but they underline the plasticity and organizational variability of functionally related regions of the eukaryotic genome and point out that we will continue to be surprised by further revelations about the degree of such diversity and mechanisms of generating it.

Poznan: Polish palaeohydrology presented

from Peter D. Moore

PALAEOHYDROLOGY is a topic which impinges upon many scientific disciplines. Physical geography, geomorphology, climatology and archaeology can all contribute to an understanding of why changes occurred in hydrological cycles in the past. Dry valleys, river palaeomeanders, the development of certain types of peat deposit, all bear witness to past conditions which may differ from those now found. To decipher such fossil geomorphological evidence and to reconstruct the hydrological conditions of past times could assist in the understanding of palaeoclimatic changes and help in seeing just how far reaching was the influence of prehistoric man upon his environment.

Poland has a long and distinguished history of research in this area and it is fitting that Poznan in Poland should form the centre for a recent conference on the palaeohydrology of the temperate zone.

L. Starkel (Krakow University) set out the complexities of this subject by showing how many varied factors have influenced the fluvial palaeoenvironment, including ice melt, sea level variation, tectonic effects and human impact. All of these have left their mark upon river patterns and sediments, thus making it difficult to evaluate the role of climatic changes. The late Pleistocene saw a change in river patterns from braided to meandering systems, which reflects lower fluvial activity following the final melting of ice and establishment of vegetation, but the trend has been interrupted on several occasions. Starkel claims that phases of increased fluvial activity recorded by such characteristics as increased grain size in fluvial deposits, more rebedded pollen and faster sedimentation rates, are synchronous over northern Europe. Periods of generally increased flood frequency occurred at 8,500-8,000, 6,800-5,800, 5,000-4,500 and 2,800-2,000 BP. All these, he claims, correspond to times of high lake levels and glacial advance, which supports the case for an overall climatic control. The increase in braiding pattern development in recent centuries, however, can be related to human activity.

It is very difficult, nevertheless, to demonstrate that any such effect is indeed purely climatic in origin. Very frequently, as discussed by K.J. Gregory (University of Southampton) and B. Frenzel (University of Stuttgart), one can detect evidence of increased human activity at precisely those times when palaeohydrological changes involving increased fluvial activity have

taken place. Forest clearance involves the reduction of transpiration rates in the vegetation and also lowers the interception of precipitation, thus permitting larger volumes of water to move through catchments into the rivers. Such evidence is often circumstantial, but its presence lays a considerable onus of proof upon those who would assert that purely climatic factors underlie the observed river changes.

Circumstantial evidence on one side can, of course, be countered by similarly based arguments on the other side. If widespread climatic changes can be demonstrated, which coincide with the fluvial palaeoevent, then this can support the climatic case. Beside evidence from glacial movements, the record supplied by pollen maps is becoming increasingly valuable, especially in the form presented by T. Webb (University of Providence, Rhode Island) who has developed transfer functions based upon modern pollen studies which allow him to translate fossil pollen maps into projected climatic ones. A similar piece of work has been conducted by N.A. Khotinsky (Moscow University) who has constructed a series of Holocene vegetation maps for the USSR, based upon fossil pollen data, which permit palaeoclimatic interpretation. Data emerging from this work may have profound implications, as, for example, the discovery of the elm decline at about 5,000 BP far beyond the supposed geographic limits of Neolithic cultures in the USSR. The case for climate (or disease?) is strengthened.

Since synchronicity is the key to these arguments, dating of deposits relating to palaeohydrological and climatic events becomes critical. This problem is particularly well demonstrated by the river channel studies of S. Kozarski (University of Poznan) in the Warta valley of central Poland. Aerial photography and geomorphological mapping have revealed the scars left by the river during the course of its development. In one location to the south of Poznan, the river once bifurcated and the valley which no longer carries the Warta River has the scars associated with a braided pattern. The main river valley shows two series of palaeomeander scars, an outer series with a mean curvature radius of 200 m and an inner series with a mean radius of 123 m. These old channels have become blocked and form oxbow lakes filled with sand and peat as swamp and fen vegetation has colonized and ultimately obscured them. The sediments at the base of the channels, however, provide evidence which is useful in determining their date of origin and hence aids the reconstruction of the history

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6. Harvey *et al.* *Nature* **294**, 49 (1981).
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8. Zernik *et al.* *Cell* **22**, 801 (1980).
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12. Chandler *et al.* *Science* **205**, 908 (1979).
13. Stephenson *et al.* *Cell* **24**, 639 (1981).
14. Childs *et al.* *Cell* **23**, 651 (1981).
15. Leder *et al.* *Nature* **293**, 196 (1981).
16. Hereford *et al.* *Cell* **18**, 1261 (1979).
17. Wallis *et al.* *Cell* **22**, 799 (1980).
18. Mitchell Smith (personal communication).

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of the river's development. Palaeobotanical evidence (from macroremains, such as fruits and seeds, and from pollen) is also helpful and has been analysed by K. Tobolski (University of Poznan).

The outer, larger series of palaeomeanders contains botanical evidence of an origin during the closing phases of the last glaciation. The pollen spectra are herb dominated and the major tree components are birch and pine. The dwarf birch (*Betula nana*), juniper, *Artemisia* and *Chenopodiaceae* all provide evidence suggestive of open, park-tundra vegetation typifying late-glacial conditions. Precise location of the sediments within the late-glacial chronology is difficult, on the palaeobotanical evidence, and one wonders whether the argument about whether the basal deposits date from before or after the Bølling Interstadial can ever be resolved on this basis. The observed changes in sediment and pollen stratigraphy could so easily be a consequence of inwash from the steep sides of the channels, thus confusing the stratification of the deposits.

Radiocarbon dating has been attempted and figures in excess of 11,000 BP have been

obtained for certain levels, but the sediments are calcareous, making the precise interpretation of such dates difficult. It is reasonable, however, to conclude that the development of the wider series of meanders (which replaced the braided system) occurred during the late-glacial. This could be accounted for by the reduced flow resulting from the completion of ice wastage, the development of a complete (and partly wooded) vegetation cover, and the possibility of reduced precipitation.

The inner series of meanders proved to be considerably younger. The pollen spectra of the basal sediments within these are tree dominated, with oak predominant. Available radio-carbon dates suggest that some of these younger palaeomeanders began forming around 4,000 years ago, and some later than this. The smaller radii suggest that more water was moving down the Warta, but whether this was a consequence of climatic changes or human deforestation is impossible to ascertain.

The enigma of man's role in the palaeohydrology of central Poland is perhaps epitomized by the remarkable excavations of an Iron Age fortified

settlement at Biskupin near Bydgoszcz. Built upon a low-lying peninsula extending into a 100 hectare lake this timber-built settlement, dating from 550 BC, has been extraordinarily well preserved as a consequence of raised lake levels swamping the wooden foundations. 35,000 stakes of oak and pine formed a palisade around the camp, which covered an area of about 2 hectares and within which were rows of wooden buildings, over 100 in all. The population was largely agricultural, growing wheat, barley, millet, beans, lentils and flax, and this arable emphasis, coupled with the timber necessary to build such a construction, must have involved extensive deforestation of the surrounding region. Which brings one back to the question of whether such forest clearance could have affected the hydrological regime in such a way as to lead to raised lake levels and the ultimate swamping of the settlement which finally led to its abandonment. Since this particular period in prehistory is generally believed to have been a time of increasing precipitation and lowered temperatures in northern Europe, this may have to remain just another palaeohydrological conundrum. □

A particularly anomalous Seyfert galaxy

from J. H. Krolik

SEYFERT GALAXIES and their quasar cousins have provided much observational mash for the vats of theoretical speculation over the years since their discovery. A recent article by T. Heckman and B. Balick¹ has thrown an especially juicy bucketful into this already potent brew. Ordinarily, what astronomers find extraordinary in these objects are the very large continuum luminosity (10^{43} – 10^{45} erg s⁻¹ in Seyferts, 10^{45} – 10^{47} erg s⁻¹ in quasars) and the very strong, broad (10^3 – 10^4 km s⁻¹) emission lines coming from an optically unresolved source believed to be no more than a few parsecs in size. In this new paper, attention is turned to extraordinary goings-on outside the nucleus of a Seyfert galaxy.

Heckman and Balick made vidicon pictures of the galaxy Markarian 335 with a series of interference filters covering bands centred on H α and [O III] λ 5007, each 3,300 km s⁻¹ wide (FWHM), and extending in total over a range $\pm 5,000$ km s⁻¹ from line centre. Most of the line emission does indeed come from the galactic nucleus, but surprisingly, there is a significant flux in most of the observed wavelength range from regions clearly separate from the nucleus. Interpreting the emission as coming from a large photoionized nebula, the inferred mass of gas outside the nucleus is $\sim 2 \times 10^8 n_e^{-1} M_\odot$ and its

kinetic energy $\sim 2 \times 10^{58} n_e^{-1}$ erg, where n_e is its electron density in cm⁻³. Such a large mass of gas moving at such high speed has never been seen elsewhere.

The first question that comes to mind is the source of ionization to drive the H α recombination radiation. Heckman and Balick check that it is plausible for the Seyfert nucleus to be supplying enough ionizing photons. Baldwin and colleagues² previously showed that the nucleus of 3C 120 superionizes its H II regions. Here the Seyfert nucleus has a much more dramatic influence on its galactic environment.

The second question is the source of the gas. An obvious supposition, and one that Heckman and Balick consider, is that this gas is material that once radiated the nuclear broad emission lines but has now spread further out into the galaxy. Unfortunately, we have no clear way of telling whether the nuclear emission line clouds travel radially in, radially out, or go in any other direction. Some lines (for example, C IV λ 1549) have profiles which are easy to measure, but are emitted isotropically, and so tell us nothing about cloud kinematics. On the other hand, those lines, such as L α , which are emitted only from one face of a cloud³ are often so distorted by blending or intervening absorption that their usefulness is destroyed. Therefore, the presence of this gas may be as good an indication that at least some Seyfert nuclei expel gas some of the time as asymmetry of nuclear emission line profiles.

Once the possibility of a nuclear origin for this gas is admitted, many other questions instantly arise. Why did the expulsion last only for 10^6 years (its kinematic age)? Seyfert galaxies are generally supposed to live at least 10^8 years. Why did it occur only in Markarian 335, a galaxy which doesn't appear remarkable in any other way (but one, which we discuss in the following paragraph). In their kiloparsecs-long passage out into the galaxy, why haven't the clouds been appreciably slowed by drag? Why is the shape of the nebula so strongly asymmetric?

The final, and perhaps most interesting, question stems from Heckman and Balick's measurement of the radial profile of the galaxy's continuum emission. They find that the surface brightness declines away from the centre in a way more characteristic of elliptical galaxies than spirals. If Markarian 335 is an elliptical galaxy, it would be the only such Seyfert galaxy known; all other Seyfert galaxies whose types have been determined are spirals. Ordinarily, when an elliptical galaxy has a line-emitting nucleus, it is also a bright radio source, which Markarian 335 is certainly not. On the other hand, Seyfert galaxies sometimes do evince small-scale radio emission near their cores⁴. VLA observations of this unusual Seyfert galaxy might be a particularly fruitful next set. □

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The 1980 geomagnetic reference field

from David R. Barraclough

GLOBAL descriptions of the geomagnetic field are useful for many scientific purposes as well as being important in navigation. Traditionally, the information has been displayed by means of charts showing isolines of the geomagnetic element in question. Whilst this is adequate and even desirable for many navigational purposes, it has disadvantages for scientific use. During the last quarter of a century mathematical models of the geomagnetic field have been produced in large numbers to meet the needs of scientists and modern World Magnetic Charts are themselves

produced using such models as the first stage in the compilation process.

In almost all cases, the modelling technique used is the expansion of the geomagnetic field in terms of spherical harmonics. In this method, pioneered by Gauss almost 150 years ago, the potential (V) from which the geomagnetic field is derivable is expressed (equation (1)) as

$$V = \alpha \sum_{n=1}^N (\alpha/r)^{n+1} \sum_{m=0}^n (g_n^m \cos m\phi + h_n^m \sin m\phi) P_n^m(\theta)$$

Here, α denotes the radius of a reference sphere, usually taken to be the mean radius

(6,371.2 km) of the Earth, r the geocentric radial distance, θ the geocentric colatitude and ϕ the longitude of the point at which the potential is to be found and $P_n^m(\theta)$ denotes the associated Legendre function of degree n and order m . For a complete description of the Earth's magnetic field the series in equation (1) should extend to $m=n=\infty$, but in practice the series is truncated at a maximum value (N) of m and n , usually in the range 8 to 15. The geomagnetic field and its components can then be derived by taking the gradient of V as given by equation (1). A spherical

Spherical harmonic coefficients of the international geomagnetic reference field 1980

		DGRF			IGRF				DGRF			IGRF	
<i>n</i>	<i>m</i>	1965 nT	1970 nT	1975 nT	1980 nT	1980-85 nT yr ⁻¹	<i>n</i>	<i>m</i>	1965 nT	1970 nT	1975 nT	1980 nT	1980-85 nT yr ⁻¹
<i>g</i>	1 0	-30,334	-30,220	-30,100	-29,988	22.4	<i>h</i>	7 6	-23	-23	-23	-23	-0.1
<i>g</i>	1 1	-2,119	-2,068	-2,013	-1,957	11.3	<i>g</i>	7 7	1	-2	-5	-2	0.0
<i>h</i>	1 1	5,776	5,737	5,675	5,606	-15.9	<i>h</i>	7 7	-12	-11	-12	-10	1.1
<i>g</i>	2 0	-1,662	-1,781	-1,902	-1,997	-18.3	<i>g</i>	8 0	13	14	14	20	0.8
<i>g</i>	2 1	2,997	3,000	3,010	3,028	3.2	<i>g</i>	8 1	5	6	6	7	-0.2
<i>h</i>	2 1	-2,016	-2,047	-2,067	-2,129	-12.7	<i>h</i>	8 1	7	7	6	7	-0.1
<i>g</i>	2 2	1,594	1,611	1,632	1,662	7.0	<i>g</i>	8 2	-4	-2	-1	1	-0.3
<i>h</i>	2 2	114	25	-68	-199	-25.2	<i>h</i>	8 2	-12	-15	-16	-18	-0.7
<i>g</i>	3 0	1,297	1,287	1,276	1,279	0.0	<i>g</i>	8 3	-14	-13	-12	-11	0.3
<i>g</i>	3 1	-2,038	-2,091	-2,144	-2,181	-6.5	<i>h</i>	8 3	9	6	4	4	0.0
<i>h</i>	3 1	-404	-366	-333	-335	0.2	<i>g</i>	8 4	0	-3	-8	-7	-0.8
<i>g</i>	3 2	1,292	1,278	1,260	1,251	-0.7	<i>h</i>	8 4	-16	-17	-19	-22	-0.8
<i>h</i>	3 2	240	251	262	271	2.7	<i>h</i>	8 5	8	5	4	4	-0.2
<i>g</i>	3 3	856	838	830	833	1.0	<i>h</i>	8 5	4	6	6	9	0.2
<i>h</i>	3 3	-165	-196	-223	-252	-7.9	<i>g</i>	8 6	-1	0	0	3	0.7
<i>g</i>	4 0	957	952	946	938	-1.4	<i>h</i>	8 6	24	21	18	16	0.2
<i>g</i>	4 1	804	800	791	783	-1.4	<i>g</i>	8 7	11	11	10	7	-0.3
<i>h</i>	4 1	148	167	191	212	4.6	<i>h</i>	8 7	-3	-6	-10	-13	-1.1
<i>g</i>	4 2	479	461	438	398	-8.2	<i>g</i>	8 8	4	3	1	-1	1.2
<i>h</i>	4 2	-269	-266	-265	-257	1.6	<i>h</i>	8 8	-17	-16	-17	-15	0.8
<i>g</i>	4 3	-390	-395	-405	-419	-1.8	<i>g</i>	9 0	8	8	7	6	
<i>h</i>	4 3	13	26	39	53	2.9	<i>g</i>	9 1	10	10	10	11	
<i>g</i>	4 4	252	234	216	199	-5.0	<i>h</i>	9 1	-22	-21	-21	-21	
<i>h</i>	4 4	-269	-279	-288	-298	0.4	<i>g</i>	9 2	2	2	2	2	
<i>g</i>	5 0	-219	-216	-218	-219	1.5	<i>h</i>	9 2	15	16	16	16	
<i>g</i>	5 1	358	359	356	357	0.4	<i>g</i>	9 3	-13	-12	-12	-12	
<i>h</i>	5 1	19	26	31	46	1.8	<i>h</i>	9 3	7	6	7	9	
<i>g</i>	5 2	254	262	264	261	-0.8	<i>g</i>	9 4	10	10	10	9	
<i>h</i>	5 2	128	139	148	149	-0.4	<i>h</i>	9 4	-4	-4	-4	-5	
<i>g</i>	5 3	-31	-42	-59	-74	-3.3	<i>g</i>	9 5	-1	-1	-1	-3	
<i>h</i>	5 3	-126	-139	-152	-150	0.0	<i>h</i>	9 5	-5	-5	-5	-7	
<i>g</i>	5 4	-157	-160	-159	-162	0.2	<i>g</i>	9 6	-1	0	-1	-1	
<i>h</i>	5 4	-97	-91	-83	-78	1.3	<i>h</i>	9 6	10	10	10	9	
<i>g</i>	5 5	-62	-56	-49	-48	1.4	<i>g</i>	9 7	5	3	4	7	
<i>h</i>	5 5	81	83	88	92	2.1	<i>h</i>	9 7	10	11	11	10	
<i>g</i>	6 0	45	43	45	49	0.4	<i>g</i>	9 8	1	1	1	1	
<i>g</i>	6 1	61	64	66	65	0.0	<i>h</i>	9 8	-4	-2	-3	-6	
<i>h</i>	6 1	-11	-12	-13	-15	-0.5	<i>g</i>	9 9	-2	-1	-2	-5	
<i>g</i>	6 2	8	15	28	42	3.4	<i>h</i>	9 9	1	1	1	2	
<i>h</i>	6 2	100	100	99	93	-1.4	<i>g</i>	10 0	-2	-3	-3	-3	
<i>g</i>	6 3	-228	-212	-198	-192	0.8	<i>g</i>	10 1	-3	-3	-3	-4	
<i>h</i>	6 3	68	72	75	71	0.0	<i>h</i>	10 1	2	1	1	1	
<i>g</i>	6 4	4	2	1	4	0.8	<i>g</i>	10 2	2	2	2	2	
<i>h</i>	6 4	-32	-37	-41	-43	-1.6	<i>h</i>	10 2	1	1	1	1	
<i>g</i>	6 5	1	3	6	14	0.3	<i>g</i>	10 3	-5	-5	-5	-5	
<i>h</i>	6 5	-8	-6	-4	-2	0.5	<i>h</i>	10 3	2	3	3	2	
<i>g</i>	6 6	-111	-112	-111	-108	-0.1	<i>g</i>	10 4	-2	-1	-2	-2	
<i>h</i>	6 6	-7	1	11	17	0.0	<i>h</i>	10 4	6	4	4	5	
<i>g</i>	7 0	75	72	71	70	-1.0	<i>g</i>	10 5	4	6	5	5	
<i>g</i>	7 1	-57	-57	-56	-59	-0.8	<i>h</i>	10 5	-4	-4	-4	-4	
<i>h</i>	7 1	-61	-70	-77	-83	-0.4	<i>g</i>	10 6	4	4	4	3	
<i>g</i>	7 2	4	1	1	2	0.4	<i>h</i>	10 6	0	0	-1	-1	
<i>h</i>	7 2	-27	-27	-26	-28	0.4	<i>g</i>	10 7	0	1	1	1	
<i>g</i>	7 3	13	14	16	20	0.5	<i>h</i>	10 7	-2	-1	-1	-2	
<i>h</i>	7 3	-2	-4	-5	-5	0.2	<i>g</i>	10 8	2	0	0	2	
<i>g</i>	7 4	-26	-22	-14	-13	1.6	<i>h</i>	10 8	3	3	3	4	
<i>h</i>	7 4	6	8	10	16	1.4	<i>g</i>	10 9	2	3	3	3	
<i>g</i>	7 5	-6	-2	0	1	0.1	<i>h</i>	10 9	0	1	1	-1	
<i>h</i>	7 5	26	23	22	18	-0.5	<i>g</i>	10 10	0	-1	-1	0	
<i>g</i>	7 6	13	13	12	11	0.1	<i>h</i>	10 10	-6	-4	-5	-6	

harmonic model of the geomagnetic field thus consists of the $N(N+2)$ coefficients g_n^m , h_n^m ($m=0, 1, 2, \dots, n$; $n=1, 2, \dots, N$) in equation (1).

Because of the relatively low truncation levels used, such models represent the parts of the geomagnetic field with wavelengths upwards of several thousand kilometres, that is, that part of the field which originates, in the main, from sources in the Earth's fluid core. This so-called main field is important in ionospheric and magnetospheric studies, in cosmic-ray physics and in studies of magnetic anomalies caused by crustal rocks. Magnetic anomalies can give valuable information about mineral resources but it is necessary to remove from the observations a realistic regional field so that the shorter wavelength crustal structure can be revealed. In the past, such regional fields were usually derived in an *ad hoc* way for each individual area of interest and this gave rise to problems when anomaly maps of adjacent areas were combined.

As an aid to users, and in particular to those interested in the study of magnetic anomalies, the International Association of Geomagnetism and Aeronomy (IAGA) adopted, in 1968, an International Geomagnetic Reference Field (IGRF) describing the main geomagnetic field at 1965 by means of 80 spherical harmonic coefficients ($N=8$). Since the field changes with time, an additional set of 80 coefficients describing the secular variation was also included to extend the period of usefulness of the model. By the early 1970s it was becoming obvious that inaccuracies in the secular variation coefficients were causing unacceptably large errors in field values computed for current epochs from the model and the IGRF was revised by IAGA in 1975. This revision was limited to the provision of a revised set of 80 secular variation coefficients to be used for deriving field values for dates after 1975, the original and revised versions of the IGRF being continuous at 1975. With the passage of time this revised model has itself become inaccurate and a second revision of the IGRF was made at the IAGA Assembly held in Edinburgh last August.

The new version of the IGRF consists of five component models: four models of the main geomagnetic field for 1965, 1970, 1975 and 1980 and a model of the secular variation valid for the interval 1980 to 1985. The four main-field models each consist of 120 coefficients ($N=10$) whilst the secular variation model has, as before, 80 coefficients. The values of the coefficients are given in the Table. The constituent models have been derived by taking weighted means of three sets of candidate models, one each from the Institute of Geological Sciences in the UK, NASA (Goddard Space Flight Center) in the USA and the United States Geological Survey. The main-field models for 1965,

1970 and 1975 are designated Definitive International Geomagnetic Reference Fields (DGRF 1965, DGRF 1970 and DGRF 1975, respectively) since further revision is not envisaged. Linear interpolation between neighbouring models is to be used for dates that lie between the epochs of the models. The main-field model for 1980 and the secular variation model for 1980–85, which together constitute IGRF 1980, will be revised at a later date, probably about 1985. For dates between 1975 and 1980 a Provisional International Geomagnetic Reference Field (PGRF 1975) is defined by linear interpolation between DGRF 1975 and the main-field coefficients of IGRF 1980. For the interval 1980 to 1985, the main-field and secular variation coefficients of IGRF 1980 are to be used, according to the expression

$$C(t) = C(1980) + \dot{C}(t-1980)$$

where t denotes the date, C a main-field coefficient and $\dot{C}$ the corresponding secular variation coefficient. All coefficients are given in the Schmidt quasi-normalized form and refer to a sphere of radius 6,371.2 km. For conversion from

geodetic to geocentric coordinates the use of the International Ellipsoid is recommended. This ellipsoid has an equatorial radius of 6378.160 km and a flattening factor of $1/298.25$.

Computer programs for synthesizing field values and coefficients of the IGRF in computer-readable form are available from the following data centres: World Digital Data Centre C1, Geomagnetism Unit, Institute of Geological Sciences, Murchison House, West Mains Road, Edinburgh EH9 2LA, UK; World Data Center A, National Oceanic and Atmospheric Administration, EDIS/NGSDC (D62), 325 Broadway, Boulder, CO 80303, USA; World Data Center A for Rockets and Satellites, Code 601, NASA/Goddard Space Flight Center, Greenbelt, MD 20771, USA.

The evaluation of the candidate models and the specification of the revised IGRF were the responsibility of Working Group I-1 (Chairman, N.W. Peddie) of IAGA.

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Meteoritics — more facts, more complexity

from R. Hutchison and C. T. Pillinger

A recent meeting of the Meteoritical Society* opened with a commemorative address for Harold Clayton Urey who died earlier this year, delivered by one of his former students, G.J. Wasserburg. The same speaker also gave the last lecture which looked into the future. His message, think isotopes and study only precisely characterized samples instead of random and heterogeneous bulk specimens, would undoubtedly have been approved of by his mentor. Meteorites are complicated objects (they seem to get more complicated all the time) recording chemical and physical processes which occurred before, during and after formation of the Solar System. They will only be divested of their information by much detailed research.

Between Wasserburg's opening and closing remarks, another former Urey student, Sam Epstein, reviewed data obtained by himself and F. Robert at Caltech concerning the deuterium/hydrogen ratios and other stable isotope compositions of the carbonaceous polymers of C1 and C2 chondrites which revealed that some fractions had several times more deuterium than terrestrial samples. This is an astounding result when compared to the parts per thousand

deuterium/hydrogen variations occurring on Earth.

Not to be outdone, N.J. McNaughton *et al.* (University of Cambridge) reported that for almost all the water extracted from bulk LL3 ordinary chondrites Bishunpur and Semarkona, the deuterium content was at least as high as that from the carbonaceous meteorites. Starting with samples like these, Urey might have made his Nobel Prize-winning discovery of deuterium a little earlier. The consensus of opinion was that deuterium enrichments are the result of ion-molecule reactions occurring in dark interstellar clouds and that a component from this source has survived within the Solar System as a heterogeneity in primitive meteorites.

Clearly, the deuterium story needs some of that painstaking effort demanded by Wasserburg. An example worth emulating is that of Ne-E, the almost pure ^{22}Ne , thought to be the daughter of short-lived ^{22}Na , which was first discovered in 1969. Thanks to the efforts of the Eberhardt group at Berne, who performed X-ray powder diffraction studies and semi-quantitative analysis during scanning electron microscopy, another of the host phases of Ne-E seems now to have been identified as a hydroxy or fluorapatite.

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* The 44th meeting of the Meteoritical Society was held at Berne, Switzerland, August 17–22, 1981.

Thus the parent ^{22}Na presumably was located in spinel¹, in a carbonaceous substance² and in apatite — the reasons for these diverse associations are not yet forthcoming.

Whilst the existence of a material which predates the Solar System is appearing more and more likely from Ne-E studies, the possibility that the Allende meteorite contains inclusions with ages up to 5,200 Myr — half a billion years older than the Solar System — appears to be receding. Employing the simple but elegant method of measuring the gas after irradiation, in a sealed ampoule, J.C. Huneke and I.M. Villa (Caltech) succeeded in showing that exceptionally high losses of ^{39}Ar (up to 65 per cent) can occur from fine grained Allende inclusions, probably by diffusion after recoil out of the fine grains into the grain boundary voids. E. Jessberger (Max-Planck-Institut für Kemphysik, Heidelberg), speaking on behalf of the group which reported the 'aged' Allende inclusions³, stated that appropriate repeat measurements would be performed with the added precaution of shielding from thermal neutrons in case these have some detrimental effect.

Changing views on the origin of Ca-Al rich inclusions in Allende and other carbonaceous chondrites were made clear by the reception given to G. Kurat's invited lecture. Eight or ten years ago, an origin by condensation was almost totally accepted for high temperature inclusions. Kurat (University of Vienna) was one of the few dissenters. Now, origins as melts, condensates and residues from evaporation are all considered, depending on the relevant chemical and textural characteristics of each.

There was much debate on the validity and refinement of estimates of cooling rates of meteorites based on different techniques⁴. Such information may be useful in determining minimum sizes for the parent planets of meteorites. K.H. Esbensen and V.F. Buchwald (Technical University of Denmark) showed that a 20 ton iron of the Cape York shower had formed by fractional crystallization from an Fe-Ni-S-P liquid down to about 700°C. Moreover, some of the products had not been significantly altered by solid state diffusion during subsequent cooling. Considerable chemical variation among the Cape York shower was described (D.J. Malvin and colleagues, UCLA), arguing against formation by simple fractional crystallization whilst part of the small planetary core thought to have been parental to all irons of group IIIAB.

R. Hutchison *et al.* (British Museum) defended their hypothesis⁵ of hot accretion

and rapid cooling for the formation of H-group chondrites, one aspect of which was questioned by J. Willis and J.I. Goldstein⁶ (Lehigh University). A discrepancy between the metallographic cooling-rate (0.5°C Myr⁻¹) and the Pu-fission cooling rate (> 3.8°C Myr⁻¹) of the Marjalahti pallasite was announced by P. Pellas and colleagues (Museum d'Histoire Naturelle, Paris). If the latter is confirmed it would remove the inconsistency of the planetary core (IIIAB irons) seeming to have cooled faster than the core/mantle interface (main group pallasites) which is its outer boundary.

The importance of recent Antarctic meteorite finds provided a recurrent theme of the meeting. Collections of samples from areas of blue ice on the Antarctic continent by US and Japanese expeditions seemed to be offering meteoriticists guaranteed employment for some time to come. As detailed studies have got under way, however, it transpires, not unexpectedly, that many samples are paired and are thus representative of meteorites which fragmented⁷. Both S.G. McKinley (Albuquerque) and M. Honda (Tokyo) provided invaluable pairing information which should save colleagues unnecessary duplication.

The recovery and mechanisms of concentration of Antarctic meteorites were discussed by L. Schultz *et al.* (Mainz) and J. Annexstad (Johnson Space Center, Houston). One factor is wind, which can blow masses of up to 20 g across bare ice, to be concentrated at the snow covered margin. Earlier hopes of obtaining a supply of unweathered meteorites from

Antarctica have been dashed over the past few years. An example was presented of a small, dark stone sitting in a pool of water, although the air temperature was -20°C! However, as long as samples are unweathered, even though they may have spent a lengthy period on the ice cap before recovery, they may be considered as uncontaminated in terms of trace elements, like museum specimens observed to fall and immediately collected and carefully preserved (M.E. Lipshutz, Purdue).

Another facet of the paper by Honda was that the terrestrial ages of Yamato meteorites range from 10⁴ to 7 × 10⁵ years, the mean life of an Antarctic meteorite probably being about 2 × 10⁵ years. Our sample of ancient meteorites from Antarctica is essentially the same as that from the rest of the world.

Several rare or unique meteorites have been recovered. H.Y. McSweeney and A.M. Reid (University of Cape Town) described the first observation in a meteorite of a contact between two primary, igneous lithologies, which probably formed in a single magma chamber. From the other side of Antarctica came a 189 g meteorite intermediate in composition between diogenites and eucrites (H. Takeda and H. Mori, Tokyo). Finally McKinley and colleagues (University of New Mexico) described a 'unique' unequilibrated, L3, chondrite from Allan Hills. The stone is unusual in that it contains both magnetite-graphite and silicates in the matrix, and so is intermediate between 'normal' unequilibrated ordinary chondrites and a recently discovered graphite-magnetite rich variety⁸. □



99 years ago

The *Japan Gazette* of August 21 contains a long and curious description of a bear festival among the Ainos. The writer, Dr. B. Scheube, is, we believe, the only European who has ever been actually present at this ceremony, the descriptions of it given by Miss Bird and other writers being derived from hearsay. The festival is now rarely held, and there is small reason to regret this, as it has degenerated to a brutal orgy. It commences with drink, every change in ceremony begins and concludes with drink, until finally every one in the village is intoxicated, while their hands, faces, and clothes are smeared with the gore of the sacrifice. Dr. Scheube says: "I had much difficulty in keeping off the drunken crowd that wanted me to partake of the blood and liver (the latter is eaten raw); and I can say that though hardened in these things by the practice of my profession, the sight of these drunken people with their bodies smeared over with blood filled me with a loathing that made me feel glad that the day and the feast were

coming to an end together". Dances, many of them of an obscene nature, also form part of the ceremony.

Mr. Stanley has published separately a full report of the address he recently gave in Paris. From this we glean one interesting item of exploration. After he had launched his steamer on the upper waters of the Congo, above the cataracts, he proceeded up the river and entered the Kwango, the great southern tributary. One hundred miles from its mouth he came to where two large streams united to form the main river; a greyish-white stream from south by east, the other, of an inky colour, from east by south. Ascending the latter, much less rapid than the former, Mr. Stanley came, after steaming another 120 miles, to a large lake, into which the river widened. On circumnavigating it, he found it about seventy miles in length, and with a breadth varying from six to thirty-eight miles. The natives he found very wild, and naturally astonished at the puffing monster. A splendid country the shore seemed to be — dense, impenetrable — lofty forests, alternating with undulating grass lands. Mr. Stanley was altogether three years away from Vivi, and doubtless he has collected much information in the country around the Congo.

From *Nature* 27, 19 & 21, November 2, 1882.

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4. Wood, J.A. in *Asteroids* (ed. Gehrels) 849 (University of Arizona Press, 1979).
5. Hutchison *et al.* *Nature* 287, 787 (1980).
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8. Rubin *et al.* *Nature* 291, 544 (1981).

AUTUMN BOOKS SUPPLEMENT

Who will write more books?

Books have an odd place in the scientific literature. The institution of the book, especially when bound in hard covers, still commands general respect. Most books, after all, are the products of hard work and devotion by one or a few people. And not merely authors but attempted authors know how lonely their work is, and how it may give hostages to fortune. Yet some books have a lasting influence. Newton's *Principia* and Darwin's *Origin of Species* are but the most conspicuous if almost hackneyed examples.

Books are also, however, widely suspected. And with some reason. Although few books are now published entirely without the benefit of external criticism, peer review does not apply as formally as to articles published in the journals. Often, indeed, the authors of books appear to shoulder responsibility for external review themselves, thanking a small group of friends for help and advice immediately before the ritual disclaimer in most prefaces that only the author should be blamed for the errors that survive. And while some publishers may take great pains to ensure that manuscripts are read with care, and revised if necessary, the procedures of formal review are not uniform either between publishers or books, and are rarely in any case explicit. This is the sense in which books are often regarded as peripheral to the scientific literature proper.

Accordingly there is a temptation among professional people to suppose that books are somehow half-way between Apocrypha and light entertainment, in contrast to the measure of respect accorded to at least some journals. Books, then, are at a disadvantage in professional esteem compared with articles in the journals — a sad reversal of the traditional opinion that printed books are in some permanent way the embodiment of scholarship. So journals now command the attention of authors, who are reluctant to put more than a few thousand words on paper. Moreover, the scorn of books as vehicles of scholarship is probably greater among scientists than among other professional scholars.

It is high time that this balance was redressed. The importance of the journals in the scientific literature will not easily be undermined, and there is no reason why it should be, whatever the prospects ahead for electronic publishing and the like: but the value of printed books, especially those by a single author or by a few close collaborators is now too little appreciated. The result is that people's natural disinclination to suffer the pains of authorship for no immediate recognition is strengthened. The symposium of reviews of books that appears on the following pages may persuade some whose disenchantment is not permanently rooted that these neglected scholarly forms do indeed require more careful nourishment.

The most important need is that the contribution of books not merely to the education of students but of contemporaries should be more widely appreciated. Although most professional people are aware in their own education of the influence of particular books which seemed at first to be a means of coming to grips with some body of knowledge, and which later turned out to be a lasting challenge, it is now all too common that students, even undergraduates, are provided not with a book but with a list of references to articles in the journals (or even, illegally, with copies of them) and invited to make up their own books in their heads. By way of justification, it is often argued that this practice not merely teaches students about their subjects but that it also enables them to understand what research is like. This, however, is a thin excuse for many teachers' laziness.

A good textbook differs from the most carefully chosen set of

references in several obvious but nevertheless crucial ways. First, it will have a sense of history that cannot be conveyed by a list of dates. Second, it will judiciously assess the importance of contributions to some field of study. But it will also be challenging, stimulating and — ideally — original. Even in the most rapidly changing fields, good books for students have an element of reflectiveness of necessity absent from articles in journals. The appearance of Feynman's *Lectures in Physics* in the 1950s was a good illustration of how the very best textbooks become required reading for fellow-teachers as well as students. But, teachers will complain, good up-to-date textbooks simply do not exist in quickly moving fields. The remedy, they must know, is in their own hands, or pens.

Another common complaint is that there are too few scholarly reviews in the scientific literature. Over the years, especially in the United States, a succession of committees has considered how to encourage working scientists to withdraw for a time from the bench or the competition for space in the ordinary journals to distil their knowledge of a field or topic into a reflective review. Several remedies have been suggested. Review journals might help. So might fees for authors. In some fields these policies have worked well, sometimes commercially — without the need of subsidy. The results are widely appreciated, not only by people reading their way into a subject but by the scientific community as a whole. Yet the argument that there should be more reviews, and that scientists should be more willing to produce them, is only a part of the much stronger argument that there is an urgent need of more books, and that they too are a charge on people's professional responsibility. For books have the advantage over journals that they are — at least soon after publication — more accessible, more portable and more memorable. But who except professional scientists can meet the need to which they so often draw attention?

These didactic goals are the bread and butter of scholarship. But are the monumental books differently conceived? Not necessarily. Newton's *Principia*, indeed, reads as if it were a textbook, with its lemmas, theorems and the like; it was, after all, intended to instruct. And it is easy to see how the *Origin of Species* might have begun as a scholarly review of what was known, in the mid-nineteenth century, of the relationships between species. But in the end the result was a thesis. The moral is that even quite pedantic exercises in authorship may turn out to help to change the world. That is part of the fun, now apparently much neglected.

For many people, however, the potential excitement of authorship is outweighed by what are often considered to be the dangers inseparable from books. For books lend themselves to reflectiveness and also, unfortunately, to discursiveness. Thus they tempt authors into subjective judgements of other people's work, even to speculation. Is that not a temptation to resist, potential authors ask themselves? And is it not in any case dangerous to be published in a format which, it is well-known, includes much unfounded speculation hung loosely on a mass of unrefereed data, unestablished assumption and tendentious argument? The implied criticisms are unfortunately occasionally applicable. The conclusion is not, however, that all books are bad but merely that some are bad. Others, everybody knows, are at the other end of the spectrum. And their absence would impoverish the scientific literature as a whole. Is it not therefore time that the scientific community stopped complaining about the scientific literature and instead set about adding to the quality of that part of it which has been most neglected in the past few decades?

The making of a modern museum

William Coleman

THE British Museum was largely the product of a single dazzling collection and the intention of an indefatigable collector, Sir Hans Sloane. Soon, however, that collection and the Will that transferred it to the British nation faced unexpected and, hindsight makes clear, increasingly unwelcome competition. Sloane had primarily collected natural objects — plants, animals and minerals — and an associated library. Late in life he proposed that these materials, suitably housed and cared for, should form a repository in which his fellow countrymen could, as Robert Hooke had earlier declared of the Royal Society's museum, "read the book of nature" itself. But conflict was inherent in the very act of creation of the British Museum (1753). Sloane's treasures were confounded with two additional and equally remarkable collections: The Cottonian library and the Harleian MSS. Here were books and documents, important artefacts of human culture, that became and remained formidable rivals of the artefacts of nature.

Until 1880 these varied materials and numerous others, particularly archaeological objects and monuments of early European civilization, slept together in crowded confines in Bloomsbury. Their coexistence pleased few. Antonio Pazzini, Principal Librarian (that is, senior executive officer), was an imperious administrator and the impassioned developer of the Museum's printed materials and manuscripts, the heart of today's British Library. Until 1856 the scientific collections possessed no comparable advocate. From that date, Richard Owen, anatomist, zoologist and skilful political manipulator, directed a course that led to the opening, on 18 April 1881, of Alfred Waterhouse's visually superb new home for the scientific collections. The move to South Kensington in 1880–1883 thus provided physical autonomy for the natural history collections; complete independence (except for its cumbersome name) came only in 1963 when Sloane's original foundation was divided and the British Museum (Natural History) acquired its own board of trustees, including a majority of scientists.

W.T. Stearn and A.E. Gunther, in dissimilar but complementary books, record in abundant detail the many and often complex developments and conflicts that produced today's British Museum (Natural History). Stearn's is a truly comprehensive

The Natural History Museum at South Kensington: A History of the British Museum (Natural History) 1753–1980. By William T. Stearn. Pp.496. ISBN 0-434-73600-7. (Heinemann: 1981.) £15. *The Founders of Science at the British Museum, 1753–1900.* By A.E. Gunther. Pp.219. ISBN 0-950-72760-1. (Halesworth, Suffolk, UK: 1980.) £9.90, \$20.

account, dealing with all aspects of the institution: Gunther explores, largely biographically, selected scientific work carried out by the staff at the Museum during its early years. Printed materials, official and unofficial reports and memoranda, correspondence and scientific publications provide the basis for these volumes. Gunther refers briefly and adequately to his sources but Stearn, alas, one of the foremost students of the bibliography of natural history, provides no overall guide to the marvellously diverse materials that he has consulted; his references lie scattered throughout the text and will need to be extracted by each reader as occasion dictates. Both volumes are well illustrated, the authors' selection of pictures affording a view of most features of the Museum's activities, including curation, exhibition and administration. Also valuable are the several appendices offered by each author, listing chronologically persons and major events associated with the Museum.

A museum, particularly a museum as important and well frequented (two to

three million visitors per annum) as is the British Museum (Natural History), constitutes a diverse and expensive institution that inevitably must try to serve many masters. Its public face may appear orderly and calm but its private life is one of sharply differing opinions and compromise, the latter often offering satisfaction to few or none. Gunther and especially Stearn provide a record of the struggles, some personal and others substantive, that have constantly beset the Museum but neither author provides a sustained general consideration of the one issue that remains in question in all seasons, namely, what are and should be the principal functions of a (natural history) museum and how are these goals best to be realized.

Preservation and exhibition of specimens were intrinsic to Sloane's conception of a national museum; the further purpose of increasing the collections in size, and ultimately in systematic diversity, was added in later years. Only slowly did the British Museum (Natural History) come to view scientific research and technical advising as part of its concern. The example and the constant urging of John Edward Gray (1800–1875) encouraged this trend, one that required appointment of a competent scientific staff. But this was a matter for long years of no particular interest on the part of the Trustees. Such concerns continue, of course, and the demands that they pose are only heightened when limitations on staff,

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A COURTESY OF THE BRITISH MUSEUM (NATURAL HISTORY)

National Darwinist Gallery

funds and space become severe. The latter is a chronic museum problem and one often felt by the British Museum (Natural History). Confusion of function has been further compounded by the perceived tastes of the television generation: museum exhibitions and popular publications admittedly seek the lower end of a vague average intellect. They seek their market, attendance having become a crucial statistic with which to defend old support and to solicit new funds, by offering gentle instruction and mounting increasingly brilliant displays. Old values have in the process been transformed and the new product — the word fits well — is perplexing.

In this world agog with educational technology and associated display techniques, one must ask a foolishly obvious question — what use the artefact itself? It was the very object whose protection was the minimal original objective of any serious natural history collection, yet many modern displays, including the “spectaculars”, offer more aluminium and plastic than rock, cellulose or flesh, however dry. Study collections, the hard core of a museum in confident times past — and today, as extinctions proceed apace, one of our few hopes for further increasing our understanding of the career of life on this globe — occupy the back room; the public is given a glance at most. The moral is obvious: as display divorces itself from artefact, so might this circus in miniature easily and effectively separate itself from a central museum. Modern displays are instructive and entertaining but they are also reproducible; they can play in Palermo or Peoria as well as in London or New York. So perhaps they should, while the central museums redirect their limited resources to the care, study and display of the genuine objects of natural history. □

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The public's view of the Natural History Museum in the 1980s. Opposite — part of the “Nature Stored: Nature Studied” exhibition, a display in a more traditional mould. Above left — the artefacts of nature remain, but push-button displays obtrude in the “Man's Place in Evolution” exhibition. What would Richard Owen (right) have made of it all?

The grand Vernonian omnibus

Robert Fox

Gentlemen of Science: Early Years of the British Association for the Advancement of Science. By Jack Morrell and Arnold Thackray. Pp. 592. ISBN 0-19-858163-7. (Oxford University Press: 1981.) £30, \$59.

THIS summer, in York, the British Association for the Advancement of Science celebrated its 150th anniversary. There could have been no more appropriate location. For it was in York, in 1831, that some 350 “friends of science” set in motion what a friendly contemporary called “the grand Vernonian omnibus”. (The reference was to the Revd William Vernon Harcourt, the son of the Archbishop of York and the central figure in the task of foundation.) By 1844, when the fourteenth of its peripatetic annual meetings took place, once again in York, the BAAS had completed a circuit of the main traditional centres of British cultural life — Oxford, Cambridge, Edinburgh and Dublin (London, then as now, being excluded as a possible venue) — and of some of the bigger industrial cities. On the way it had given unprecedented visibility to the scientific enterprise and signally advanced the incipient sense of community among Britain's men of science. Oxonians and Cantabs, manufacturers and clergy, military men and doctors, peers and politicians, even some women, had become united in an organization whose seemingly easy commitment to the value-free universalism of science in reality carried a carefully constructed ideology.

Gentlemen of Science is a meticulous study of the first 13 years of the BAAS, in

which these successes were achieved. They were decisive years for science in Britain: the neologism “scientist” won acceptance, and more importantly, as Morrell and Thackray argue, the very *idea* of science as a distinct form of knowledge, at once benign, powerful and progressive, was articulated. In the process, Harcourt's Baconian conception of the Association as a vehicle for the predominantly empirical work of his fellow provincials gave way to a rival conception, emanating from London and Cambridge, which stressed the primacy of theory and mathematics. Inexorably, it seems, the intellectual weight of the Association drifted towards Section A (mathematical and physical science), and it was in mathematical physics that the early BAAS established its most distinctive and coherent tradition of research. Moreover, as mathematical physics rose in the BAAS hierarchy of the sciences, the biological and social sciences — agriculture, ethnology and geography, for example — fell, while phrenology and education were among the would-be sciences that were edged out altogether. Even medicine succumbed as the Association's leaders took upon themselves the task of defining “science”: it was no coincidence that the medical section disappeared in 1848.

The waters which the BAAS chose to sail were often choppy. Tractarians and fundamentalists joined the most conservative elements in political life in seeing the organization as a rival claimant to the various areas of authority which they regarded as their preserve. Then there was always the problem of competing interests within its

ranks. How, in particular, did it find room for two such abrasive and mutually hostile personalities as Sir David Brewster and William Whewell, the former virtually unemployed and obsessed with the inadequacy of scientific patronage, the latter basking in the ample luxury of Trinity College, Cambridge? One answer seems to lie in the prosopography of the twenty Gentlemen of Science whom Morrell and Thackray identify as the ruling coterie of the BAAS (and who give the book its title). All but two of the twenty were Anglicans of a liberal or latitudinarian persuasion, and most of them were also Whigs or Peelites Tories with an interest in moderate reform. They were, in short, predominantly men of the centre, wedded to an ideal of conciliation and social harmony.

It is one of the most impressive achievements of this impressive book to relate the spirit of accommodation which pervaded the higher reaches of the BAAS to the political and social conditions of the troubled decades that separated the massacre of Peterloo (1819) from the Chartist National Assembly of 1848. With mob violence a real or potential threat, and with established institutions being questioned as never before, there was every

reason for the gentry and aristocracy to feel beleaguered. They needed allies, and so reached down the social scale to make common cause with an increasingly powerful educated middle class which shared the aristocracy's horror of wholesale revolution. In this quest for social integration, science was quickly recognized as a natural field for shared endeavour, if only because it was deemed to be of such varied utility, whether as uncontroversial rational amusement, as the foundation of Britain's industrial prowess (a particularly dubious claim at the time) or as the source of at least a limited understanding of God. After two or three decades in which, for all these reasons, the vogue for science had gripped polite society, in metropolis and provinces alike, the conditions for the success of the BAAS could hardly have been more auspicious.

Gentlemen of Science is the fruit of more than ten years of painstaking research, in the course of which thousands of previously unknown letters (300 of them soon to be published in the Royal Historical Society's *Camden* series) have been culled to exciting effect. The authors bear their immense erudition gracefully, ingeniously mingling detailed narrative with passages

of analysis, and succeeding brilliantly (where so many others have failed) in elucidating the constant interplay between the content of scientific knowledge and the context of its production. The book bristles with challenging interpretations. If only by implication, it tilts effectively at the *canard*, launched by contemporary Jeremiahs like Charles Babbage and still alive to this day, according to which British science about 1830 was in decline. Babbage was, of course, correct in stating that science in Britain did not have the level of state patronage that it enjoyed in France. But what he did not say was that many French *savants* were in turn envious of Britain's tradition of self-help. That the French were justified in their envy is made abundantly clear by Morrell and Thackray's account of the BAAS's achievements, whether as a forum for the discussion and dissemination of ideas or as a lobby in what was at the time the new game of hunting research grants.

At last the early history of the BAAS seems to make sense. Above all, it is to be hoped that historians will never again try to squeeze the devotees of British science in the 1830s and 1840s into the uncomfortable strait-jacket of conventional models of professionalization. The aim of the Gentlemen of Science was not the advancement of science as a means of livelihood; they regarded the study of nature as a vocation whose interests were more likely to be harmed than served by the fetters of full-time scientific employment. Hence there was nothing paradoxical about their enthusiasm for colourful public displays, ranging from the sparkling dinner which the Archbishop of York offered at his palace during the 1831 meeting, to the impromptu sermon which Adam Sedgwick delivered "to some 3000 or 4000 colliers and rabble" on the beach at Tynemouth (Newcastle upon Tyne meeting, 1838). There was nothing paradoxical either about the fact that independent men of science like the Marquis of Northampton and the retired stockbroker Francis Baily occupied as prominent a place in the BAAS leadership as university chairholders like Sedgwick, Whewell and Baden Powell. By their work for the BAAS, these men undoubtedly contributed to the establishment of science as a profession. But they did so unwittingly. Had they been at York this year, they would have marvelled at our modern paraphernalia of formal qualifications and rigid career-patterns. They might also have reflected that science is no longer quite the *fun* which this absorbing and entertaining book shows it was 150 years ago. □

Robert Fox is Reader in the History of Science at the University of Lancaster and President of the British Society for the History of Science. His most recent book, co-edited with George Weisz, is The Organization of Science and Technology in France, 1808-1914 (Cambridge University Press, 1980).

DINNER

GIVEN BY THE

Magistrates & Town Council of Glasgow LIST OF TOASTS.

- | | |
|--|-------------------------|
| 1. THE QUEEN, | CHAIR. |
| 2. Prince Albert, | Do. |
| 3. The Queen-Dowager and the rest of the Royal Family, | Do. |
| 4. The Army and Navy, | Do. |
| 5. The British Association & the Marquis of Breadalbane, | Do. |
| 6. The City of Glasgow, and the Lord Provost and Magistrates, | MARQUIS OF BREADALBANE. |
| 7. The University of Glasgow, and Principal M'Farlan, | LORD BELHAVEN. |
| 8. The Scientific Institutions and Societies of Europe and America, | PRINCIPAL M'FARLAN. |
| 9. The Memory of James Watt, and the other eminent men of Great Britain who have contributed to the Advancement of Science, | GENERAL TSCHIEFFKINE. |
| 10. The Noblemen and Gentlemen from other parts of the Kingdom, who have honoured this Meeting of the British Association with their presence, | SIR JOHN ROBISON. |
| 11. The Astronomers of the Continent, and Mr. Encke, | PROFESSOR AIRY. |
| 12. The Royal Society, and its Noble Chairman, the Marquis of Northampton, | MR. ENCKE. |
| 13. The Foreigners who have contributed so much to the interest and success of this Meeting of the British Association, | MARQUIS OF NORTHAMPTON. |
| 14. The Ladies who have honoured the Meeting by attending its Sections, | DR. BUCKLAND. |
| 15. Railway Communication, & other Improvements which tend to facilitate intercourse between mankind, and thereby promote friendly relations, | LORD SANDON. |
| 16. The Members for the City, | CROUPIER. |
| 17. The Rajah of Travancore, the great Promoter of Science in the East, | SIR D. BREWSTER. |
| 18. The Commercial and Manufacturing interests of the Country, which owe so much to Science for their advancement, | LORD MONTEAGLE. |
| 19. Foreign Naturalists, and M. Agassiz, | MR. LYELL. |
| 20. The Lord Lieutenant of the County, | |
| 21. The Secretaries of the British Association, | |
| 22. The Local Officers for the Glasgow Meeting of the Association, | MR. PHILLIPS. |

For the early members of the BA science was perhaps more fun than it is today, but must have had its tedious aspects. The illustration shows the list of toasts proposed at a dinner given for the Association by Glasgow Corporation in 1840.

In search of our place in the Universe

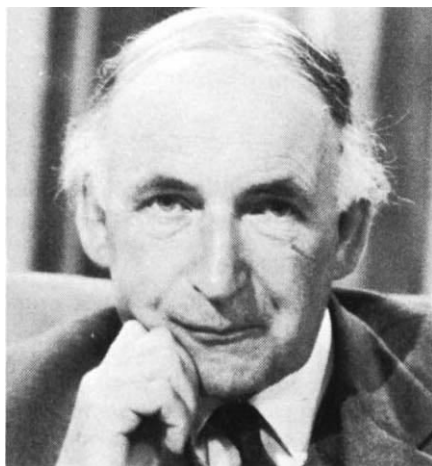
Joseph Silk

PHILOSOPHERS arise! Cosmology is beckoning. For mankind has found a niche in the Universe as it expands from an origin shrouded in mystery to an unknown future. Sir Bernard Lovell's new book tells the story of the development of human awareness of the Universe. Lovell leads us from the geocentric cosmology of the ancient world via the heliocentric cosmology of the Renaissance and the egocentric cosmology of the nineteenth century. His destination, of course, is the big bang theory of the expanding Universe, where fundamental issues still await resolution. Some of these issues differ little from the questions which faced the cosmologists of antiquity. Sir Bernard Lovell is an eminent radioastronomer who has no cosmological axe to grind, and it is especially refreshing to discover that his popular account of the evolution of cosmology manages to be both readable and enthralling.

We learn about the epicycles of Hipparchus and Ptolemy, and about how Thomas Aquinas incorporated Aristotle's crystal sphere cosmology into an apparently irrefutable argument for the existence of God. With Copernicus, the heliocentric hypothesis re-emerged and, against all odds, survived, while Tycho Brahe established the first accurate and systematic records of planetary data. Brahe punctured the immutable crystal spheres with his studies of comets and of the famous supernova of 1572. His assistant, Johannes Kepler, derived the laws of planetary motion after a painful decade of sifting endless mathematical permutations of the planetary data, and despite unflinching belief in the celestial harmony exhibited by the five regular solids. Next, Galileo's observations with a 4 cm aperture telescope caused an immense stir that led to an unavoidable conflict with the geocentric dogma upheld by theologians. Galileo saw sunspots, the moons of Jupiter and the phases of Venus, all of which established that the heliocentric system was a reality, and could no longer be thought of as a computationally convenient hypothesis. It remained for Isaac Newton to express the universal law of gravitation in a way that gave a theoretical understanding of Kepler's Laws.

The stage was set for modern astronomy. One of the great pioneers was William Herschel, who counted stars and mapped our Milky Way galaxy. Not, however, until the twentieth century was the Sun finally displaced from the centre of the Universe. Harlow Shapley resoundingly overthrew the egocentric view of the place of mankind in the Universe by using the newly calibrated period-luminosity relation for Cepheid variable stars to establish distances to remote globular star clusters. These were found to surround the

Emerging Cosmology. By Bernard Lovell. Pp.208. ISBN 0-231-05304-5. (Columbia University Press: 1981.) \$14.95, £10.80.



Sir Bernard Lovell, now tackling the history and philosophy of cosmology.

centre of our galaxy some 30,000 light years from the Sun. Much happened subsequently: the discoveries of the expansion of the Universe and of the cosmic microwave background radiation are two of the highlights that have now led cosmologists almost unanimously to adopt the big bang cosmological model.

All of this forms a backdrop to Lovell's theme, which is the evolution of cosmological thinking. Lovell's book forms part of a philosophical series entitled "Convergence" and founded, planned and edited by Ruth Nanda Anshen in order to explore the new consciousness which marks mankind's recently acquired ability to tinker with the evolutionary processes of nature. Our unfolding knowledge of the cosmos traditionally places cosmologists in the role of passive observers acquiescing in the thrill of new astronomical explorations of the frontiers of the Universe. Unlike most natural scientists, astronomers cannot perform controlled experiments in a warm laboratory; rather they take whatever the Universe has to offer.

One might think that such a discipline would have little in common with philosophers who concern themselves with the interaction between human beings and their environment. However a current cosmological theme provides a remarkable bridge between the philosophical undertones associated with the origin and fate of the Universe and the human perspective. This is the anthropic principle, according to which the properties of the Universe are determined by our presence as observers. Conditions must be congenial for intelligent life to evolve. This means, for example, that the early Universe could not have been highly irregular, inhomogeneous or chaotic, nor however could it have been perfectly regular, otherwise galaxies

and stars would not have formed. The anthropic principle accounts for the various large-number coincidences involving powers of 10^{40} , the ratio of electromagnetic to gravitational coupling constants. These include the mass of a star and the mass of the observable Universe, as well as the coincidence between nuclear, stellar and Hubble expansion time-scales. It even purports to account for the approximate values of the constants of nature: if they differed significantly from observed values, human beings could not have evolved.

Where does this leave us? The uniqueness of our Universe can be attributed to our existence as observers, if we accept the anthropic principle. But have we really advanced our understanding of any aspects of cosmology? In 1925, A.N. Whitehead perceived about cosmology that "there is no parting from your own shadow". Is the Universe merely our shadow? Or perhaps the cosmologists are deceiving themselves and the roles are reversed. The truth may very well be that with only one Universe to explore, we can never resolve this paradox.

Joseph Silk is Professor of Astronomy at the University of California, Berkeley, and author of *The Big Bang* (W.H. Freeman, 1980).

All around our star

David W. Hughes

The New Solar System. Edited by J. Kelly Beatty, Brian O'Leary and Andrew Chaikin. Pp.224. ISBN 0-521-23881-1. (Cambridge University Press: 1981.) £9.95, \$19.95. *Orbiting the Sun: Planets and Satellites of the Solar System.* By Fred L. Whipple. Pp.338. ISBN 0-674-64125-6. (Harvard University Press: 1981.) \$20, £14. *Daytime Star: The Story of Our Sun.* By Simon Mitton. Pp.191. ISBN US 0-684-16840-5; ISBN UK 0-571-11659-0. (Charles Scribner's Sons/Faber & Faber: 1981.) \$14.95, £10.

WE LIVE in the Solar System. Our planet, Earth, orbits the Sun and the theme of these three books seems to be that the more we know of such bodies the better. In effect we are presented with a progress report. Governments have spent large amounts of money on investigating our neighbouring planets and star. What have we got from it? Where do we go next? Why bother doing more? The books under review try to answer these questions.

The investigation of the Solar System has passed through three phases. The classical period encompassed the works of scientists such as Galileo, Copernicus, Kepler and Newton. This was a time of discovery and astronomy was almost entirely concerned with the planets, stars being

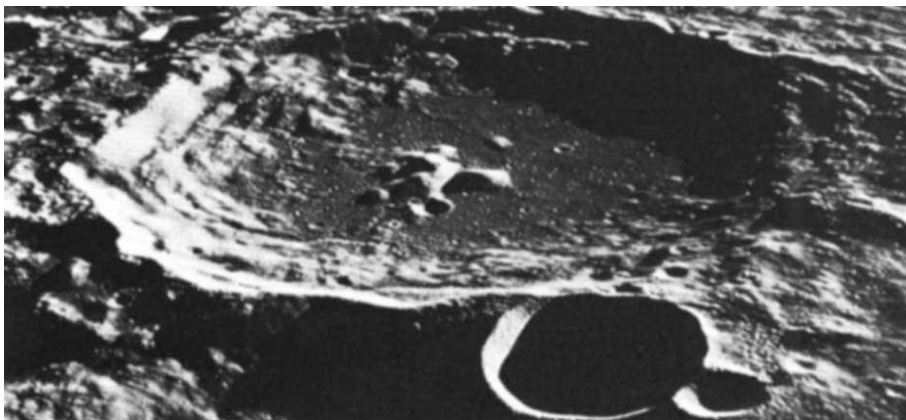
fixed points of light of little known significance. The second phase started in the late 1800s when astrophotography and spectroscopy spawned the discipline of astrophysics. During this period planetary investigation degenerated into a Cinderella science. The early 1960s saw the dawn of planetology. Since then spacecraft have been flung round, onto and into all of the planets known to the ancients, producing a veritable explosion of knowledge.

The first book under review is *The New Solar System*. Very rarely does one come across such an excellent account; I feel honoured to have a first edition as it is bound to run to many printings. The editors have collected together 20 chapters, each of about ten pages, written by a roll call of American scientists which reads like a *Who's Who* of US planetology. It is invidious to omit names, but as an indication of the standard it includes Eddy on the Sun, Chapman on asteroids, Burns on planetary rings, Wood on meteorites, Masursky on Mars, Shoemaker on the role of fragmentation and so on. The book concentrates on the comparative approach. It is much easier to discuss the surfaces of the terrestrial planets (Mercury, Venus, Earth and Mars) in one chapter and, for example, their atmospheres in another than to have an isolationist attitude to individual planets.

The joy of reading the book is greatly enhanced by the illustrations. Not only does it bulge with space photographs, but it also contains a collection of coloured illustrations by artists Charles Wheeler, Don Davies and Jon Lomberg.

The editor's aim was to provide a book about the third phase of planetary exploration, the space-age planets, a book which would make enjoyable reading for those with either a professional or a casual interest. They have succeeded admirably. The fact that the publishers have produced this large format, beautifully illustrated, quality book at less than £10 is verging on the miraculous. I advise all readers to buy it.

The second book is Fred Whipple's *Orbiting the Sun: Planets and Satellites of the Solar System*. This is a completely revised and updated edition of Whipple's classic text, *Earth, Moon and Planets*, which was first published in 1941. Whipple is Philips Professor of Astronomy, Emeritus, at Harvard University and Senior Scientist, Emeritus, at the Smithsonian Institution Astrophysical Observatory. He has devoted his life to the study of astronomy and space science, especially meteors, comets, space exploration planning, satellite tracking, novae and supernovae, Solar System evolution and practical astronomy; it is fascinating to read the view of such a man about the place of Earth and Moon within the planetary context. Whipple writes for the general reader and mathematics are avoided; however, the book does present the basic foundation of planetary astronomy and



The crater Daedalus on the far side of the Moon, photographed by Armstrong and Aldrin on July 21, 1969. The picture is taken from *The Atlas of the Universe* by Patrick Moore, a new edition of which has just been published by Mitchell Beazley, price £19.95.

does stress the underlying scientific principles. The author has also managed to integrate the three phases of Solar System investigation and we realize that all still have a role to play. We might move from bleary telescope images to the eye-opening, crisp detail of the space probe, but the Earth-based telescopes have recently revealed Pluto's moon, the rings of Uranus and Apollo asteroids. Also we realize that stars and planets are not to be compartmentalized. Whipple leaves us in no doubt that the origins and deaths of stars are intricately connected with the origin and evolution of our planetary system. The book is well written, well illustrated, well worth reading and a worthy successor to the previous editions.

My final book is *Daytime Star: the Story of Our Sun* by Simon Mitton. The word "Story" in the title describes the book well — Mitton dives into the subject and returns with a net bulging with intrigues. Why did ancient man worship the Sun and build stone circles to track its path? What drives the sunspots? Does the solar energy output vary slightly and thus trigger ice ages? What do neutrinos tell us about the solar interior? What have we learnt from space

about the solar atmosphere? Mitton has a racy style and we find atomic particles sloshing, neutrons bashing, gases toasting and gravity crunching.

There is much to be learnt about the Sun from this book, and it fills a definite gap in the astronomical library of the general reader. The author worried me when he stated that in 1964 "the finding of the solar wind was a result of astronomical observations of extremely remote radio sources", but 86 pages later he changes his mind and Biermann's 1951–1953 observations of comet tail phenomena are given the credit. I also found that the position of the Sun in the stellar hierarchy needed much more emphasis and that it is not enough just to say that the Sun has "an average size, typical mass, normal structure, temperature and luminosity". Granted the Sun is on the Main Sequence but it is also about nine times more massive than the average star and about 2,000 times more luminous. But these are minor quibbles about a book which is generally of a high standard and is definitely a good read. □

David W. Hughes is a Lecturer in Astronomy and Physics at the University of Sheffield.

The philosophy of astronomical discovery

David S. Evans

Cosmic Discovery: The Search, Scope, and Heritage of Astronomy. By Martin Harwit. Pp.334. ISBN UK 0-7108-0089-4; ISBN US 0-465-01428-3. (Harvester Press, Brighton/Basic Books, New York: 1981.) £12.95, \$25.

IN the blurb Sir Fred Hoyle describes *Cosmic Discovery* as "A remarkable book. A unique book". So it is. It is an examination of the epistemology of astronomy, and one of those books which will set astronomers and philosophers thinking and talking. It is not a book which will command general acquiescence. Exactly how much influence it will have is hard to

say since it is certainly not everybody's cup of tea.

It starts off, oddly enough, with an idea connected with the collection of baseball cards. If one finds a duplicate, the set must be finite and if at any stage one counts up the number of single different cards (A) and the number of duplicates (B) the size of the set (n) may be estimated from the statistical formula $n = A(A + 2B)/2B$. Harwit then applies this to astronomical discoveries of which he considers there are 43 distinct ones, and of these seven are recognized in two different ways. He is very careful about defining what he means by different ways, that is by totally unrelated

techniques, perhaps best illustrated by the fact that the existence of galaxies was recognized by optical observations, but would now independently be found from radio observations. Putting $A = 35$, $B = 7$ in 1979, with one triply recognized phenomenon ($C = 1$), he estimates that there are 123 separate cosmic phenomena to be found of which we have now recognized 35 per cent. From a discussion of the rate of discovery he thinks we might know all of them by 2150 AD, a somewhat depressing conclusion for those who love observational astronomy, though favourable error bars would increase the numbers and postpone the date. Harwit distinguishes between original discoveries and their development, so that our successors may not all be unemployed by then.

He builds upon a figure published by Halton Arp in 1965 which defines the limitations of observations of extended visual sources considered in terms of their absolute magnitudes and linear diameters. In an elaborate analysis of techniques he considers the parameters of possible detection methods — frequency, size, spectral resolution, time resolution, ellipticity of polarization and intensity — and constructs multidimensional phase diagrams to show what is now accessible and what might become accessible in the future, and classifies each of his fundamental discoveries according to this scheme.

One chapter outlines his selected set of phenomena and the circumstances of their discovery. He makes a number of points in passing — for example that new discoveries follow the introduction of new techniques, with which few readers will quarrel. However he tends to think only of revolutions in techniques rather than in their availability. To an observer one of the most important events of the past few decades was the identification by Thackeray and Wesselink of both Cepheids and RR Lyrae stars in the Magellanic Clouds because of the newly available 74-inch reflector in the Southern Hemisphere. The resultant doubling of the scale of the Universe does not rank in his list of 43 discoveries. He mentions the serendipity of many discoveries, but fails to mention the outstanding discovery by John B. Irwin that S Normae was a member of the cluster NGC 6087. In fact his accounts of pulsating variables and flare stars leave a good deal to be desired and he fails to mention that pulsations continue down even into the white dwarf range. Indeed, one has the impression that in his accounts of fundamental discoveries Harwit confines himself to data from a rather restricted selection of well-known sources, especially those closest to the NASA publicity machine. For example, in his remarks on pulsars we fail to find any mention of the names of Cocke, Disney, Taylor, Nather or Warner, and the name of Lundmark is omitted from the story of the identification of the 1054 AD supernova remnant. The independent observation of

the Uranus rings by Joseph Churms gets no mention. Among other distinguished absentees, de Vaucouleurs rates no inclusion for the discovery of the local supergalaxy.

Though one can quarrel with Harwit's selection of phenomena and his historical accounts, perhaps this will not invalidate his main thesis for some readers. He remarks that many of the discoverers were not originally trained as astronomers, which is true but easily explained. The basic discoveries in radio, X-ray or gamma-ray astronomy were made before anybody could describe himself as an astronomer specializing in these fields. Until a few decades ago, employment opportunities in astronomy were so few that even aspirant astronomers took care to have an employable skill in some other field as a hedge against failure in the discipline of first choice. He remarks that by his reckoning the major proportion of recent discoveries has been made by Americans, though he might have added that even now a high proportion of top posts in American astronomy are held by individuals whose original training was received elsewhere, apparently himself included.

Lastly, he notes that many of the most original discoveries have been made by individuals outside the main stream of astronomical organization and funding. This, of course, has been remarked in other sciences; one can command organized research but it seems impossible to command true originality. However, insofar as observational astronomers in all fields are now married to large and expensive instruments, detailed planning and allocation of resources is essential.

The last part of the book contains Harwit's message — "How should we organize astronomy?". He argues for 13 recommendations, many of which are obvious enough — better training in physics and mid-career training in new techniques for astronomers, and vigorous introduction of exponents of new techniques in astronomy. Long-term grants will better allow astronomers to address fundamental problems and the current peer review system must be loosened up to encourage true innovation, "which can seldom be justified in advance". On the other hand, projects should not be kept on just because they have gone on for a long time. He wishes to encourage gravitational wave and neutrino astronomy and believes that in the electromagnetic domain current observing capabilities could be increased by a factor of 1,000 at modest cost. He finishes with a plea for policy to be set by panels of generalists of "unusual breadth of interest and far-ranging vision", more frequent policy reviews and frequent analyses of the factors which contribute to astronomical success.

These are fine words, but how to implement them in the real world with limited funds for pure research is another matter. In view of Harwit's desire to have more

frequent review committees, it is odd that he admits that "there is no evidence . . . that astronomical planning committees have in any way advanced the rate at which new astronomical phenomena are discovered . . .". This is the paradox: astronomers need to spend a lot of money, much from public sources, and need to be accountable. They can guarantee the addition of large amounts of extremely valuable knowledge from their efforts. But the history of science demonstrates two things. One is that those who have predicted the exhaustion of the results of research have usually been proven wrong, however logical their arguments. The other is that discoveries of real originality are most often made by people who ignore the basic plan and pursue their own hunches. Many of them are rightly written off as cranks, but those who succeed are geniuses.

David S. Evans is a former Associate Director for Research at the McDonald Observatory and currently a Professor of Astronomy at the University of Texas at Austin.

Relativity for all

D.J. Raine

Discovering Relativity for Yourself. By Sam Lilley. Pp.425. ISBN hbk 0-521-23038-1; ISBN pbk 0-521-29780-X. (Cambridge University Press: 1981.) Hbk £17.50, \$49.50; pbk £7.95, \$19.95.

ONE approach to physical science for the intelligent but innumerate layman is through analogy and example, omitting the why and wherefore. Sam Lilley has a different approach. He believes that students can be taught how to work things out for themselves.

Schopenhauer opined that mathematical truths properly presented can, in any case, be grasped intuitively, thereby circumventing the aridity of the Euclidean mode, for which he gave as sole justification a pictogram proof of Pythagoras's theorem. Lilley has a beautiful extension of this to the invariance of the interval in special relativity. But, even when only elementary mathematics is involved, not everything can be presented so easily; for example, on p.74 we must digress from space-time diagrams to explain negative numbers.

With general relativity the difficulties multiply. The equivalence principle is

The latest edition of *The Milky Way* by Bart and Priscilla Bok has just been published by Harvard University Press. The book, which first appeared in 1941 and has now been revised for the fifth time, costs £14.

discussed well in terms of accelerated observers in special relativity. But to master Lilley's "near equations" seems to require as much effort as would elementary calculus proper. Some limitations of the approach are apparent from the author's speculations on an alternative theory. This is incompatible with the precession of Mercury, but the reader (or author) is not provided with the confidence to do the relevant short calculation. Nor does one get any feeling for the results of the theory in cosmology, black holes or gravitational waves.

There are some mistakes: for example, a too-simple proof that bodies cannot move with the speed of light, and a peculiar notion of covariant tensors, which arises from confusing two meanings of "covariant". And amongst the more serious errors, two incompatible equations for the same gravitational force arise from an inconsistent approximation.

But for me the achievement outweighs these flaws of execution. Of the greatest importance is the demonstration, through a large number of well-made teaching points, that mathematics, the language of science, is available to anyone with sufficient motivation and the right guide.

D.J. Raine is a Lecturer in Theoretical Astrophysics at the University of Leicester. His books include Einstein and Relativity (Priory Press, 1975) and The Isotropic Universe (Adam Hilger, 1981).

From the shadows, everyman's Maxwell

R.V. Jones

James Clerk Maxwell: A Biography. By Ivan Tolstoy. Pp.194. ISBN 0-86241-010-X. (Canongate, Edinburgh: 1981.) £9.95.

For many years there hung in one of the corridors of the Electrical Laboratory at Oxford a photographic portrait of someone whom none of the staff could identify. Presumably it had been placed there by the Professor of Physics, J.S.E. Townsend; but after his death, the identity of the portrait was forgotten. It was, in fact, of James Clerk Maxwell.

Maxwell has been almost as little known in his native Scotland, where his memory has been heavily overshadowed by that of Kelvin — and this despite the fact that Einstein himself credited Maxwell with having brought about the greatest revolution in physics since the time of Newton. Not only did Maxwell create the electromagnetic theory which led to the discovery of radio waves and of electromagnetic radiation pressure, but he also formulated his distribution law governing the molecular velocities in gases, the basis of automatic control theory and the principles of kinematic design; and he demonstrated the first colour photograph.

The current year has seen the one hundred and fiftieth anniversary of his birth on 13 June 1831, while less than two years ago there occurred the centenary of his death. The commemoration of these anniversaries has coincided with increasingly wide-spread recognition of his tremendous contributions, and with papers and books describing aspects of his life and work, notably C.W.F. Everitt's short but carefully written biography (Charles Scribner's Sons, 1975) and the exhibition of Maxwell memorabilia at last year's Royal Society conversation.

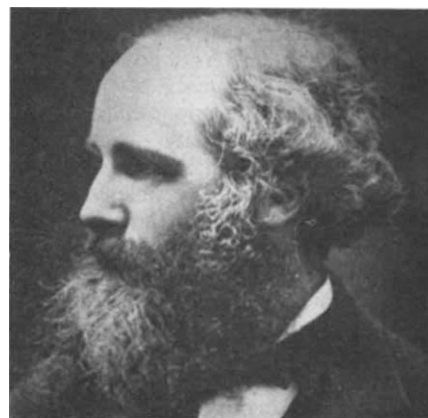
Now we are presented with another short and very readable biography, by Ivan Tolstoy, who in his preface sets out his objective:

For physicists the name of James Clerk Maxwell ranks next to Newton and Einstein. Yet among non-scientific people Maxwell's image is surprisingly faint. It is hoped the present book will help remedy that injustice. This pretends neither to be a definitive biography, nor a work of historical scholarship. It is, rather, a book for the lay reader.

Even so, and although the author has, as he says, drawn largely on secondary sources, more specialist readers will find that he has thrown shafts of light on Maxwell's character and methods of working. And in well-drawn quotations from Maxwell's own writings he has followed one of his subject's own precepts:

It is a great advantage to the student of any subject to read the original memoirs of that subject, for science is always most completely assimilated in the nascent state.

One of the rare points in the book which could be questioned concerns the process by which Maxwell came to conceive the famous displacement current in a vacuum. Tolstoy says that "There could be no physical or logical justification for keeping the concept in the context of a vacuum". This might be true if Maxwell regarded a vacuum as containing absolutely nothing, but in his 1864 paper he stated his belief in "an aethereal medium filling space" and in its having a "small but real density"; and he evidently retained this view throughout his work, for towards the end of the *Treatise* of 1873 he repeated "We must therefore regard the medium as having a finite density" (para.782). So Maxwell's train of thought was both physical and logical.



James Clerk Maxwell, the portrait that hung in the Electrical Laboratory at Oxford.

Tolstoy remarks elsewhere that "Both Einstein and Maxwell were stronger in physical intuition than in mathematics", which struck an immediate resonance in my memory with something Einstein said in conversation with F.A. Lindemann during his visit to Oxford in 1931. He was commenting on the popular description of himself as a mathematician: "I am not a mathematician. I am a physicist — if I had been a mathematician I could not have done what I have". But, of course, both Einstein and Maxwell had an impressive command of mathematics when they needed it, and Maxwell was outstandingly strong in geometrical reasoning.

Tolstoy's short account is both penetrating and sympathetic regarding Maxwell's personal relationships, of which it gives a warmly human picture; and it contains many thoughtful comments on Maxwell's physics and the context in which his advances were made. It is a book well worth reading. □

R.V. Jones is Professor in the Department of Natural Philosophy at the University of Aberdeen, and author of The Complete Physicist: James Clerk Maxwell 1831-1879 (Yearbook of the Royal Society of Edinburgh, 5-23; 1980).

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Where is everybody? Some new answers

Gerard K. O'Neill

Are We Alone? The Possibility of Extraterrestrial Civilizations. By Robert T. Rood and James S. Trefil. Pp.262. ISBN 0-684-16826-X. (Charles Scribner's Sons: 1981.) \$14.95.

IS THE origin of life so extraordinarily improbable an event that it has occurred but once in the history of our galaxy, or do star-systems other than our own teem with intelligent life, able to communicate with us? Surely this question, raised almost 40 years ago by Enrico Fermi, is one of the most profound that we can imagine.

In an engaging and readable book, Rood and Trefil outline an emerging modern view of the answer. Their style is informal and unpretentious, and the level is suitable for interested non-scientists, but they offer tid-bits of detail for specialists. Given the provocative and necessarily speculative nature of their subject-matter, it seems a happy choice on their part, as well as an honest one, that they include a chapter listing their own divergences of opinion and the arguments made on either side of the issues.

They begin with the seminal paper, "Searching for Interstellar Communications", by Giuseppe Cocconi and Philip Morrison, which appeared in *Nature* in 1959 (184, 844-846). There the authors pointed out that sensitive radio receivers could detect signals from transmitters of moderate power over interstellar distances. Frank Drake, already thinking along similar lines, was further stimulated by Cocconi and Morrison's paper and carried out Project Ozma, using a radiotelescope to listen for possible artificial signals emitted from the nearby, solar-type Tau Ceti and Epsilon Eridani systems. Although no recognizably artificial interstellar signals were ever detected, then or in searches over the succeeding decades, there grew in the early 1960s something of a consensus among those scientists interested in the question. It was based on the assumptions they made of probabilities: that a star will have planets, that life will develop on one such planet, that it will develop technological expertise and that a culture capable of communication will survive long enough to be heard. Those probabilities and a few other factors, simply multiplied together, form what is variously called the Sagan-Drake, the Drake or the Green Bank Equation. Rood and Trefil choose the last version, as a memorial to the first scientific conference (1961) on interstellar communication. The participants at the Green Bank conference concluded that intelligent life was abundant in our galaxy, that physical space-travel over interstellar distances would be forever impractical and that communication could occur only by radio transmissions; the only problem was to find the right frequency and the signal code.

One definite signal, unmistakably intelligent and extraterrestrial, could end the argument at any time, but until that happens everyone can speculate. Most of *Are We Alone?* is devoted to the fascinating skein of logic woven over the past ten years by a younger generation of scientists, who have reached a fairly general agreement among themselves that the Green Bank participants were both too sanguine on their probabilities and too short-sighted on technical progress. In the modern view, life is a far more unlikely phenomenon than had once been thought, and there is a strong possibility that it is unique to our planet.

Michael Hart stimulated much of the new research on the Fermi question, and the authors discuss Hart's work in considerable detail. Dr Hart, now at Trinity College in Texas, set up a mathematical model of the Earth's atmosphere, and in 1978 traced the evolution of that atmosphere by computer over geological time, from its formation by volcano emissions to its complete transformation through biochemical processes once life had formed. Hart found that the survival and evolution of life depended on an extraordinarily lucky series of accidents, by which the temperature of the Earth remained remarkably constant for most of the age of our planet. Had we not been so fortunate as to be located at precisely the right distance from the Sun, within margins of no more than one or two per cent, Earth would now be as lifeless as Mars or Venus, according to Hart's calculations.

The young revolutionaries further conclude that their elders were badly

The opening lines of the seminal paper by Cocconi and Morrison (1959) which stimulated others to listen for signals from space.

No theories yet exist which enable a reliable estimate of the probabilities of (1) planet formation; (2) origin of life; (3) evolution of societies possessing advanced scientific capabilities. In the absence of such theories, our environment suggests that stars of the main sequence with a lifetime of many billions of years can possess planets, that of a small set of such planets two (Earth and very probably Mars) support life, that life on one such planet includes a society recently capable of considerable scientific investigation. The lifetime of such societies is not known; but it seems unwarranted to deny that among such societies some might maintain themselves for times very long compared to the time of human history, perhaps for times comparable with geological time. It follows, then, that near some star rather like the Sun there are civilizations with scientific interests and with technical possibilities much greater than those now available to us.

misled by (in my phrase) "temporal chauvinism", a lack of appreciation of the probable development of technology beyond our era. If there is a civilization more advanced than our own, it will be ahead not just by decades but by millenia — and with technology to match. The authors conclude that the modern concept of space colonies, not published until more than a decade after the Green Bank conference, logically confounds many of the assumptions made at the time. Space colonies, they estimate, are certainly feasible technically, do not require a particularly high level of technology, and have such extraordinarily high survival value for any civilization reaching its nuclear age that they will inevitably be developed by any long-lived civilization capable of interstellar radio communication. Given the certainty of space colonies, virtually every star-system is a hospitable target for colonization by any species, no matter what its point of origin or requirements of temperature, gravity and atmosphere.

The development of space colonies therefore means, in the opinion of the young scientists of the modern school, that physical interstellar travel, first by robot probes and then by living colonists, is a natural and not particularly difficult stage in the development of any intelligent civilization. That conclusion is made quantitative by computer simulations carried out by Eric M. Jones at the Los Alamos Scientific Laboratory. Dr Jones comes to a single conclusion, remarkably insensitive to assumptions about ship speeds, the gestation time for a civilization around a star before it spawns colonies to move on to other stars, and other variables. He finds that the spread of a civilization outward across the entire galaxy takes no more than at most a few thousandths of the galactic age — that is, the expansion is explosive. My own calculations confirm that conclusion, and suggest an even shorter expansion time, less than one ten-thousandth of the galactic age. I argue that the outward movement of self-replicating robot probes is more certain than that of life, but Jones may well be right in his assertion that, in our own case, "The human migrants will not be far behind the probes".

In the view of the young revolutionaries, based on that chain of logic, if there had ever been an intelligent race prior to our own its descendants would be here already. And as we seem to have evolved locally, we are not they. Hence, there's a strong probability that we are in fact alone in our galaxy. It is thought-provoking that Enrico Fermi, by his famous question "Where is everybody?" appears to have arrived at the same conclusion 40 years earlier. □

Gerard K. O'Neill is Professor of Physics at Princeton University and President of the Space Studies Institute. His new book 2081 (Simon and Schuster/Jonathan Cape; 1981) explores the impact of technology on the human prospect.

Snow: reflections on physics in our time

H.B.G. Casimir

The Physicists: A Generation that Changed the World. By C.P. Snow. Pp.192. ISBN UK 0-333-3228-2; ISBN US 0-316-80221-2. (Macmillan, London/Little, Brown: 1981.) £8.95, \$15.95.

ALTHOUGH physicists like to insist that they are anything but narrow-minded specialists, only few of us have been professionally successful outside the field of science. C.P. Snow was one such *rara avis*. After an honourable career at Cambridge as a research fellow and later as a tutor at Christ's College, he became famous as a novelist and, moreover, distinguished himself as a Civil Service Commissioner. In his well-known Rede Lecture of 1959 he stressed the gap between "Two Cultures" but he himself tried to bridge that gap — his novels have given many readers a better understanding of the attitudes and aspirations of academic scientists.

In the present book, the first draft of which was completed just before his death on 1 July 1980, Lord Snow returns to science. In eleven chapters he depicts in broad strokes the stupendous development of physics during our century, tells about the main contributors to that development, explains its decisive influence on human society and dwells on the moral responsibility of scientists. In addition there are three appendices: Snow's farsighted editorial in *Discovery* of September

1939; Einstein's letter to President Roosevelt; and Snow's speech on the moral un-neutrality of science, delivered in 1960 to the American Association for the Advancement of Science. The book is abundantly illustrated with well chosen photographs and diagrams.

Most physicists will agree with the general tenor and with the message of Snow's book. Also, as was to be expected, Snow writes clearly and fluently, and he often succeeds in characterizing a physicist in a few pregnant sentences, for instance Fermi on p.79:

He had been recognized very young as one of the physicists of the century, and the only one who could work on equal terms with the greatest in both theory and experiment. There had been no one like that for generations . . . If Fermi had been born thirty years earlier, it was possible to imagine him discovering Rutherford's nucleus, and then proceeding to Bohr's theory of the atom. . . . As a professional scientist, not as a cosmic thinker such as Einstein or Bohr, he was one of the very greatest.

William Cooper tells us in his introduction that Snow intended to write mainly from memory and it is clear that the book is not based on careful historical studies. It is a personal narrative, but a personal narrative by a man like Snow is well worth reading. For a physicist it is stimulating to compare Snow's choice and evaluation — often based on close acquaintance with the persons and the

subjects discussed — with one's own views. But a general reader should realize that Snow's presentation is often incomplete and may lead to a one-sided or even distorted picture: it is an interesting but not entirely reliable guide.

There is, for instance, no indication of the important role of kinetic theory and statistical mechanics in the development of the atomic theory of matter; Boltzmann is not mentioned, Gibbs only as the creator of chemical thermodynamics. Einstein's work in this field passes unnoticed also. Yet it was Perrin's experimental confirmation of Einstein's predictions concerning Brownian motion that convinced many unbelievers of the real existence of atoms. Similarly, Einstein's theory of the specific heat of solids at low temperatures convinced many physicists of the reality of quantization. When writing about crystallography and X-rays, Snow mentions W.L. Bragg (Sir Lawrence) and Bernal, but fails to mention Bragg's father (Sir William) and von Laue. Wave mechanics is called the De Broglie-Schrödinger theory; that is fair, but note of the curious fact that both De Broglie and Schrödinger did not accept — or did so only with reluctance — Born's interpretation of the wave function as a probability amplitude should not have been omitted. Snow draws a lively picture of Feynman and sketches his work on quantum electrodynamics. Dyson is also mentioned, Schwinger and Tomonaga are not.

Sometimes the Cambridge (or more generally the British) point of view does not apply elsewhere. When Snow writes on p.42 "Until the Second World War there was little industrial support for physicists" this may have been true in England but in the United States, in Germany and also in my own country industry employed many physicists, some of them even Nobel Prize winners. Further, at Cambridge spectroscopy was considered to lie outside the main compass of physics. Elsewhere it was felt that Rutherford and his school were pioneering an as yet lonely track, whereas the main action was to be found in the unravelling of spectra, which indeed eventually led to the understanding of the periodic system, to the exclusion principle, to the notion of electronic spin and to the semi-quantitative vector model, thus paving the way for quantum mechanics. It was in the 1930s, after the birth of quantum mechanics, that nuclear physics burst into full bloom.

The book contains a number of plain errors, which Snow, had he lived, would presumably have corrected, and which a careful editor ought to have noticed. Uhlenbeck (p.113) was not involved in the mission of Goudsmit; the Göttingen Nobel Prize winner James Franck is turned into Josef (p.117) and the index lists both James and the non-existent Josef; A.H. Compton was an American, not a British Nobel Laureate (p.120). It was not Gell-Mann



Germany in 1933 — students and Nazis burning books by foreign and Jewish authors. The slogan reads "German students march against the un-German intellect". Such scenes led to the flight of Jewish physicists from Germany and eventually to the development of the atomic bomb in the United States.

who introduced group theory into physics (p.145): that had been done by Wigner in the late 1920s. Group theory then became one of the customary tools of theoretical physicists. Gell-Mann applied it ingeniously and successfully to the problems of particle physics.

In two cases Snow's tendency to sum up people in a few sentences leads to injustice. On p.112 he states bluntly that "General Groves was a singularly bad choice for his job". I have no well-founded personal opinion, but I notice that A.H. Compton writes in his *Atomic Quest* — by a curious coincidence also on p.112 — "The nation was fortunate indeed in the selection of General Groves for this task". Also, it cannot be denied that Groves's short-term mission was efficiently accomplished. The second case is worse. On p.26 Snow writes

... Lenard who, incidentally, as an old man was one of the only two eminent German scientists who became active spokesmen for the Nazi faith. (The other was Werner Heisenberg, a great theoretician ...).

Such parenthetic calumny should not go uncorrected. Certainly, Heisenberg was a German patriot. He loved his country; the German language and German culture meant much to him (but in the early 1920s the *Jugendbewegung* to which he belonged was not a nationalistic group). We may regret that he let his love for his country prevail over his objections to the Nazis, we may wish that he had taken a firmer and more courageous stand against them. And I admit that on the one occasion I met him during the war he showed little



C.P. Snow 1905–1981

understanding for the feelings of people in an occupied country. But he always maintained his integrity as a physicist and at one time he was even under severe attack by members of the Lenard group, because he continued to express his belief in quantum theory and relativity. It is utterly wrong to mention him in one breath with Lenard.

Nevertheless, despite these detailed criticisms, I consider *The Physicists* a valuable book. Its theme is important, its basic structure sound and it contains many incisive remarks and interesting side-lights. I read it with pleasure and profit, and am convinced that many will do likewise. □

H.B.G. Casimir studied theoretical physics at Leiden, Copenhagen and Zürich, worked in low temperature physics at Leiden and later joined the Philips Company at Eindhoven. He is a foreign member of the Royal Society and a former President of the European Physical Society.

Philosophy in an uncertain world

John Polkinghorne

Divine and Contingent Order. By Thomas F. Torrance. Pp.162. ISBN 0-19-826658-8. (Oxford University Press: 1981.) £9.50, \$27.59.

PROFESSOR Tom Torrance is a distinguished theologian, the chief apostle in this country of Karl Barth, whom many would regard as the most significant figure in twentieth-century theology. In addition, Torrance is one of the few British theologians to have taken a serious interest in what science has to say about the world. This reflects itself in Torrance's strongly objectivist approach to theology, and it is no accident that one of his best known books is called *Theological Science*.

His latest work is concerned with the assessment of the significance of the contingency that we find in nature. We can distinguish at least four senses in which such contingency is present: (i) The laws of nature are not necessary, in the sense that their form cannot be determined by pure thought alone but has to be obtained from experimental observation. The recognition and exploitation of this is what gave

modern science its superiority over that of the ancient world. (ii) The parameters appearing in those laws, such as the fine structure constant, take values which can only be determined empirically. Sir Arthur Eddington tried to deny this in *Fundamental Theory* and came to grief. However an interesting gloss on the values of these constants is provided by the anthropic principle which recognizes limitations to be satisfied in a universe in which we can emerge as observers. Torrance only mentions this in a footnote; it deserved greater consideration on his part. (iii) In the great diversity of things that happen there are unforeseeable concatenations of circumstance. This is the "chance" that Monod saw operating in the emergence of life and which for him (but not for me) caused the fabric of significance to crumble. (iv) There is the radical unpredictability of quantum mechanical observation and (I would say) the action of the will, both topics which we do not understand very well.

It seems important to discriminate between these four aspects of contingency,

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but I did not feel that Torrance always adequately observed the distinction.

As a matter of historical fact the Christian doctrine of creation helped men to recognize (i) and (ii) and so made possible the scientific revolution. By a curious twist, the Newtonian mechanical world view then tended to abolish the recognition of (iii) and (iv).

The presence of contingency in the world is combined with a high degree of intelligibility which enables us to understand it. Torrance says "The intelligibility of the universe provides science with its confidence but the contingency of the universe provides science with its challenge" (p.58). Such a view of the world is certainly consistent with the doctrine that it is the work of the sovereign will of the Creator and that its rationality is the reflection of his mind. Torrance seems to argue that only such a doctrine is possible but I cannot agree that there is that degree of intellectual compulsion. He sees creation as implying two complementary aspects. First, the world is wholly dependent on God since without his sustaining it would collapse back into nothingness. From this comes its contingent order. Second, the world is other than God (no pantheism!) so that he has made it to stand apart from him. The first aspect is the concern of theology; the second that of science whose method is to proceed *etsi deus non daretur*, as if God did not exist. A true understanding requires a synthesis of these aspects.

A test of any world view is its understanding of evil. Torrance equates evil with disorder but nevertheless (rightly I believe) does not go along with Augustine and Aquinas in seeing it as just the absence of good. I thought his discussion needed a more thorough-going eschatological dimension. Also, I did not always recognize the world of science as Torrance described it. He attributes a release from the shackles of Newtonian necessity to the creation of the field concept and to the genius of Einstein. I cannot see that. Partial differential equations have propagation properties as rigorous as those of ordinary differential equations and causality finds its place within the light-cone of relativistic physics. Further, I did not understand his attitude to mathematics. He does not like to accord it true intellectual independence (that would be dangerously Platonic and Plato's ideas are possible rivals to God in his eyes) so he says it has a "natural bond with nature". Again, I do not see that.

The book is written in a style which might be described as "Scottish professorial", a sort of intellectual cousin to the elaborate castellation of Scottish baronial. Certainly, it does not make for easy reading or rapid assimilation. □

John Polkinghorne, formerly Professor of Mathematical Physics at Cambridge, is a Fellow of Trinity College and an Anglican clergyman.

How not to make a splash in science

Robert Ubell

Polywater. By Felix Franks. Pp.208. ISBN 0-262-06073-6. (MIT Press: 1981.) \$15, £9.30.

In the early 1960s in an obscure laboratory in Kostroma, 190 miles from Moscow on the upper Volga, an equally obscure research scientist, Nikolai Fedaykin, stumbled on a surprising phenomenon. Looking at how liquids behave in very narrow capillaries, he watched as a dense new liquid formed in neighbouring empty tubes.

In Moscow, the renowned physical chemist B.V. Deryagin quickly recognized the possible implications of Fedaykin's "discovery" and took it for his own. He set an entire laboratory to work on it, published results widely and campaigned for the recognition of anomalous water at Faraday Society and Gordon Research conferences. The new liquid was 15 times denser than normal water, boiled at temperatures much higher than 100°C and froze, without forming ordinary ice, at under -30°C. For a time, Western scientists either yawned or sneered. Some guessed it wasn't water at all, but the result of contamination. Yet excitement grew, and in England attempts were made to replicate the Russian work. J.D. Bernal, in private, called Deryagin's achievement

"the most important physical-chemical discovery of this century".

The US Office of Naval Research jumped in next, sensing that the mysterious new form of water might have military uses. Ripples of interest swelled to waves: the liquid was given a name — polywater — and busy scientists suddenly found the time and money to work on what they had seen as a mere curiosity the previous week. Respected researchers and the overzealous alike scrambled to make their mark, even though, at most, only a few drops of polywater had ever been collected.

In 1973 the bubble burst. In a brief, dignified note in *Nature*, Deryagin reported that he and his colleagues had finally found it impossible to grow polywater from ordinary water. The unique qualities claimed earlier "should be attributed to impurities rather than to the existence of polymeric water molecules". The emperor was not well dressed.

Felix Franks escaped the perils of the polywater controversy, but as a distinguished surface chemist and an authority on water he was close enough to record it all. The result is this book. To his great credit, Franks treats those who believed and those who didn't with an even hand, praising little, blaming less. This is a skilfully made book, wise, urbane,

Nature of "Anomalous Water"

MANY experiments have corroborated the phenomenon involving the formation of condensates with anomalous properties from the vapours of water and other liquids on silicate surfaces. But the nature of this phenomenon remained obscure for a long time and widely differing hypotheses were put forward to clarify it, one of them involving the formation of stable associates of water molecules $(H_2O)_n$. This hypothesis was first formulated by us¹⁻⁴ and was developed further by Lippincott *et al.*^{5,6}.

We have established that there are no condensates both free of impurity atoms and simultaneously exhibiting anomalous properties. Consequently, these properties should be attributed to impurities rather than to the existence of polymeric water molecules.

Consequently, the anomalous properties of condensates may be explained, not by the formation of a new modification of water, as was previously supposed, but by the peculiar features of a reaction taking place between the vapour and solid surfaces in the process of condensation. Many aspects of the mechanism of formation of anomalous condensates have not yet been fully clarified. This especially applies to the formation of anomalous condensate on MgO surfaces^{19,20}. Only the general features of the phenomenon are clear as yet; thorough investigation by those studying processes involving the interaction of vapours and solid surfaces is clearly required.

The Institute of Physical Chemistry,
USSR Academy of Sciences

B. V. DERJAGUIN
N. V. CHURAEV

The end of polywater. Extracts from the paper by Deryagin (Derjaguin) and Churaev, published in *Nature* on August 17, 1973.

amusing. For outsiders, Franks pencils in a deft, accessible guide to what is known about water, reveals how scientists communicate with each other and offers some serious and not-so-serious asides. Especially rich are the press reports — Franks finds fault with popular magazines and newspapers for inflaming an already hot scientific debate.

Recognizing that it is easier to reconstruct history than to learn from it, Franks, nonetheless, attempts the exercise. One lesson is that since competition is the driving wedge behind science, the race for

priority created the polywater episode; other bumbles like it are inevitable, given enough money and freedom. But competition may not be essential. Other ways of getting results may be just as good, if not better. We know that there is an opposing tendency for investigators to collaborate, rather than beat each other to the punch. Competition, like polywater, may be merely an artefact of our times. □

Robert Ubell is the American Publisher of Nature. During the "polywater years" he was Editor-in-Chief at Plenum, where both Felix Franks and B. V. Deryagin were his authors.

Enchaining the power of catalysis

Herman Mark

The Chain Straighteners. Fruitful Innovation: The Discovery of Linear and Stereoregular Synthetic Polymers. By Frank M. McMillan. Pp.207. ISBN 0-333-25929-7. (Macmillan Press, London: 1981.) £17.

THE steady and slowly moving mainstream of science and technology is occasionally interrupted and enlivened by unexpected events which accelerate it and eventually change its direction into new and hitherto inaccessible domains. Popularly known as "breakthroughs", such drastic evolutions have, since the last war, occurred in mathematics through the advent of electronic computers, in physics as a result of nucleonics and laser optics and, probably best known, in the life sciences through the discovery of helices in the structure of proteins and of double helices in that of nucleic acids. This book relates in a captivating and intriguing manner the story of another breakthrough which occurred in the mid-1950s in organic chemistry and the closely related field of polymer science and technology.

It started in the late 1940s when Dr Karl Ziegler, then Professor of Organic Chemistry at the University of Halle on the Saale, became Director of the Max Planck Institute for Coal Research in West Germany. Ziegler, already a well known and distinguished scientist at that time, had worked for years on a family of substances at the border of inorganic and organic chemistry known as metallorganic compounds and had specifically concentrated his efforts on the alkyl derivatives of aluminium. One particularly representative member of this family, triethylaluminium, is a colourless, volatile liquid, highly flammable and even explosive, requiring extreme skill in its preparation and handling. But these problems, a consequence of its high reactivity, attracted Ziegler rather than deterred him; and his experimental virtuosity allowed him to dominate this field for a number of years. In the early 1950s he observed that ethylene could be added to triethylalum-

inium in such a manner that hydrocarbon chains from 10 to 20 carbon atoms were obtained. Ethylene was, at that time, a readily available and inexpensive raw material of the petroleum industry and the resulting aliphatic chain compounds were valuable starting materials for detergents, emulsifiers and plasticizers. No wonder that several chemical companies — for instance, the Montecatini Company in Italy — started to negotiate with Ziegler about a joint evaluation of his invention. Evidently his new process was interesting and useful.

But the real sensation came a year later. As a result of a strange sequence of trial and error steps, Ziegler and his associates found that through the addition to the aluminiumalkyl of heavy metal salts ethylene could be rapidly transformed into linear, high molecular weight polyethylene. Even though there already existed a well established commercial process — the ICI process — for the production of a non-linear and somewhat softer type of polyethylene, and even though a linear polyethylene — Marlex of the Philips Petroleum Company — was on the verge of becoming commercial, the Ziegler discovery acted like a bombshell. The complete novelty of the catalytic system, the mild conditions of the polymerization and the resulting simplicity of the equipment produced a rarely experienced rush of licences for the new process. Careful laboratory work with difficult materials, intuitive appraisal of unexpected results and energetic pursuit of all available avenues had created a new tool for the polymer chemist — the Ziegler catalysts — and started a new and important branch of polymer technology.

But, to the delight and surprise of the reader, this is only part of the story of the book. Dr Giulio Natta, directing the Chemistry Department of the Polytechnic Institute of Milan, happened to be a consultant for the Montecatini Company and, in due course, became familiar with the existence of Ziegler catalysts. He applied

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The Nobel Prize winners — Ziegler (left) and Natta listen as Professor Fredga makes the presentation speech, Stockholm, 1963.

them on propylene instead of on ethylene and, of course, obtained polypropylene. Considering that, at that time, no high polymers of propylene were known, this was an important contribution to polymer technology. It was dwarfed, however, by Natta's discovery that the use of Ziegler catalysts

permitted the preparation of several species of polypropylene and other vinylpolymers differing from each other only by the steric arrangement of the substituents. Until that time stereospecific catalytic power had only been observed with natural enzymes: it is understandable, therefore, that the discovery of the existence of dozens of stereo-regulated polymers and their precise identification added to this commercial

success a major scientific sensation.

Dr Frank McMillan, as a contemporary of all these events, was manager of a large industrial research laboratory and has, therefore, acquired a special feeling for the intricate relationship between fundamental research and practical application.

Needless to say, the alluring commercial features of the new catalysts and their novel applications attracted, with increasing intensity, the interest of many large companies. As a result of their permanent and strong participation, there came the day when the predominant question was formulated: "What belongs to whom?" — a question which has been debated for the last 25 years. Understandably, the litigations have led to several confrontations, and in this domain the author is a true master of ceremonies, distributing fame and blame with restraint and distinction. All this makes excellent reading: entertaining, instructive and sometimes even philosophical. In several instances he offers specific warnings to avoid certain mistakes in research and development and even in the recording of results. The clarity of his exposition should certainly convince readers to avoid such mistakes in future. But, very probably, in doing so, they will make others. □

Herman Mark is Dean Emeritus of the Polytechnic Institute of New York. At the time of the discoveries described in the book, he was in contact with two institutes in Germany and Italy and contributed some ideas to the mechanism of Ziegler-Natta polymerization.

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OLD SCIENCE
& MEDICINE



Jean Baptiste Rousseau revisited

Gunther S. Stent

The Double-Edged Helix: Science in the Real World. By Liebe F. Cavalieri. Pp.196. ISBN 0-231-05306-1. (Columbia University Press: 1981.) \$14.95, £10.80.

THE latter-day metamorphosis of molecular biology from the esoteric speciality of a small band of *aficionados* into an academic juggernaut and billion-dollar industry, and its technical and moral implications, have not been slow to draw the attention of sociologists and ethicists of contemporary science. Indeed, the writing of books about the banishment of molecular biology from the Garden of Eden has become a minor cottage industry. *The Double-Edged Helix* by Liebe F. Cavalieri, a biochemist working at the New York Sloan-Kettering Institute for Cancer Research, is another contribution to this literature. Subtitled *Science in the Real World*, Cavalieri's book addresses the politics of the recent controversy surrounding the development of recombinant DNA technology. One of his chap-

ters is entitled "Rousseau Revisited", and since Cavalieri makes no allusion to Jean Jacques, the philosopher, he appears to be revisiting Jean Baptiste, the poet, who was prosecuted and exiled from France in 1712 for libelling his colleagues.

As presented by Cavalieri, the situation is as follows. There are some people who believe that genetic engineering by recombinant DNA methods is dangerous and should be closely controlled. They are "thoughtful", "unusually frank" and "valiant"; they "have a conscience", "question neatly" and "testify" before government bodies "in the public interest". Other people, by contrast, believe that there is little or no danger in this enterprise and oppose strict controls on recombinant DNA research. They are "simplistic", "self-serving" and make "crusades"; they have "myopic vision" and form part of the "power structure", "smack of scientific elitism" and "lobby" before government bodies, "snowing" them with "massive campaigns" to satisfy "spurious" and "inane" needs.

Moreover, many of these opponents of strict controls happen to be holders of the Nobel Prize, "an exceedingly dangerous device" that gives each of them "virtual limitless power . . . within his institution and among his colleagues"; others are merely members of the National Academy of Sciences, that "tends to favor special interests", "does not represent the bulk of the national science effort" and has a president, or "high priest", who "muddies the water" and "breaches . . . canons of scientific propriety". I think there is little chance that many readers of *Nature* will find merit in this book. But it may be useful all the same to dissect and review briefly Cavalieri's main propositions.

1. Molecular-genetic engineering is morally wrong because "the natural gene pool of the earth [is] an inalienable birth-right". Moreover, we must not cross the "natural genetic barrier between species which protects the integrity of the species", as is generally done in recombinant DNA experiments. This is not a political argument, as Cavalieri thinks it is, but a theological, non-utilitarian one that has meaning only within the Judeo-Christian tradition. Since God has obviously permitted the natural gene pool of the Earth to change over evolutionary time and allowed man to change it since Neolithic times, this proposition, if true, would present us with another paradox of theodicy. In any case, what it is we are and are not allowed to do genetically hinges on the hermeneutics of Genesis 1:26 versus Genesis 2:7 and the sense in which God gave man dominion over the animals. Hence the discussion must focus on whether or not our divine grant of "dominion" includes permission to alter the natural gene pool and cross species barriers. Genesis 9:1 is relevant here, in that the passengers of Noah's Ark provide the exegetically pertinent explanation of "species". And as regards species crossing, Cavalieri's proposition is supported by Leviticus 19:19: "Thou shalt not let thy cattle gender with diverse kind; thou shalt not sow thy field with mingled seed". I believe it is possible to produce a rational argument according to which a devout Jew, Christian or Muslim should not undertake recombinant DNA experiments. In a secular context, however, the gene pool and species-crossing proposition is irrational.

2. Molecular-genetic engineering is potentially very dangerous, and hence should not be carried out, or, at least, should be closely controlled. This utilitarian argument is the centrepiece of the *The Double-Edged Helix* and, although it can be simply stated, it is actually quite complex. First, as far as the dangers themselves are concerned, they can be subdivided into short term — "immediate biohazards that could result from a laboratory accident" — and the long term — "irreversibility of the organisms themselves and the irreversible socioeconomic entrenchment that will result from the

successful use of recombinant organisms, regardless of their side effects". As for the immediate biohazards, there seems to be no disagreement regarding the possibility that such hazards *may* exist. What is under dispute is who, if anyone, is competent to assess these hazards and decide whether there is or is not a reasonable chance of averting them.

According to Cavalieri, the molecular biologists who are actually engaged in genetic engineering cannot be trusted to make this assessment, because their self-interest causes them — Nobel Laureates, Academy members and just plain bench workers — to make dishonest risk appraisals and use their "clout" to sink even the timid guidelines by means of which prudent government administrators and legislative bodies sought to protect the common weal. So it is left to investigative reporters, consumer and environmental protection organizations, and "social-responsibility-in-science" groups, whom Cavalieri cites mainly in support of his arguments, to identify the substantial biohazards associated with recombinant DNA. Of just what these hazards actually consist is, however, not — probably for lack of expertise — clearly or credibly spelled out. If Cavalieri's low opinion of the moral fibre of what he calls the "science community" were an accurate perception, the real world, being deprived of reliable expert opinion on vital scientific matters, would really be in serious trouble.

Fortunately I can recognize the scenario that has the legion of molecular biologists currently engaged in research using recombinant DNA techniques, carelessly risking the survival of mankind to satisfy their idle curiosity or venal cupidity, as merely a paranoid fantasy.

As for the long-term hazards, Cavalieri finds that in them lie "the most serious dangers of recombinant DNA technology". But, of just what these serious dangers consist Cavalieri spells out even less clearly than he does for the short-term biohazards. He merely points to the history of twentieth-century technology, which shows that many developments originally thought to be benign later turned out to have unanticipated malign side-effects. Thus Cavalieri calls on the journalist John Lear to remind us that Henry Ford's invention of the mass-produced automobile, though it provided mobility to Everyman, turned out to deprive him of a livable habitat. And Cavalieri wants us to "remember the nuclear spills, and how we were reassured about the safety of nuclear power plants". So how *does* "the irreversible socioeconomic entrenchment of recombinant organisms" present a long-term danger? Because it will

provide technological fixes for past failures that cannot be rooted out at the source. Thus we try to find a technique for curing lung cancer while we continue to . . . advertise cigarettes, and we develop oil-eating bacteria to clean up oil spills,

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instead of redesigning oil tankers or re-examining our energy-intensive and wasteful economy or making a serious effort to shift to renewable and ubiquitous energy sources.

That in the socialist countries, where there is no advertising, cigarette consumption is even higher than in the capitalist world, and that work is already in progress to produce genetically engineered microbes intended to provide a renewable energy source which would do away with oil tankers altogether, is apparently not known to Cavalieri. But for him the most ominous long-term hazard is the application of recombinant DNA techniques to the human genome. He admits that there is the possibility of performing "gene therapy" on a number of hereditary defects. But Cavalieri finds that it is not "a high priority line of research to be chosen in preference to other directions" and its benefits pale in comparison with the spectre of eugenics, which "received considerable support from industrialists like the Harrimans, Kelloggs and Carnegies". Though "its demise was aided by the repugnancy of emerging Nazism . . . with the development of new genetic techniques the eugenics movement in America could rise again".

To this it can be said, first, that whereas it is true that the project of improving the human "gene pool" by eugenic methods has fascinated many prominent geneticists, it is also a fact that despite the long-time availability of techniques (such as artificial insemination) for implementing eugenic goals by methods more humane than those practised in Nazi Germany, wide-scale eugenics has not come into use in any democratic society. So, there seems to be a firm (probably religiously rooted) resistance to eugenics, leaving its advocacy mainly to scientific cranks. Second, and more importantly, it may be the case that any answer to "the classical question: who decides what is a defect?" could lead to procedures "clearly open to abuse". But, all the same, opposing on those grounds the use of diagnostic, prophylactic and corrective procedures in medical genetics reveals a lack of genuine empathy with and concern for people in the real world, since there are hereditary disorders that every person would judge to be defects with which no human being ought to be born. Thus Cavalieri's argument against genetic engineering from long-term hazards consists merely of general cant about Henry Ford, nuclear spills and the Nazis, and puts forward no specific prognosis that can be critically examined and discussed. Rather, just as does the argument from immediate biohazards, this argument, too, merely indicates a radical lack of faith in the honesty and wisdom of the leaders responsible for the management of our democratic society and of our scientific colleagues.

3. The potential benefits of molecular-genetic engineering are too small to offset the enormous risks. "The now familiar list of potential benefits that may accrue from

recombinant DNA includes . . . the production of insulin . . . antibiotics . . . vitamins and hormones . . . and . . . food crops. . . . Do we need them?". Cavalieri answers "no". As for insulin, a "thoughtful approach to the problem of diabetes . . . was given by Harvard's Professor Ruth Hubbard" who declared insulin to be a "technological gimmick". She counsels that we should rather try to find "the causes of diabetes, which are, as with all other diseases, heavily influenced by social and environmental factors". And as for antibiotics, vitamins and hormones, in the United States we have already 20,000 pharmaceutical products in medical use, when "the World Health Organization has indicated that only 210 drugs would be sufficient to fill world health needs". And as for food crops, "we must not let our understandable sympathy for the hungry people of the world lead us into mistaking the cause of the problem, which is not one of production or quality but of distribution and utilization. The world now produces enough grain to feed everyone adequately". That is to say, abundant food is available to feed the hungry, if only the nations with undernourished populations would organize better politically and economically so that they can buy food from the affluent countries that waste their food surpluses anyhow. So "no real need has yet been brought forward to justify the serious ecological hazards of introducing major disturbances into the complex balance of things" by recombinant DNA methodology.

It is not necessary here to enter into a dis-

cussion of the merits of Cavalieri's claims. For even if these claims were just, the finitude of his list of potential benefits and his additional pronouncement that "we are no longer in an area when practical applications of scientific research are unforeseeable and the human consequences unknown" show a demagogic refusal to allow that what is sauce for the goose is also sauce for the gander. If it is the case that, as Cavalieri claims elsewhere, history teaches us that the long-term *hazards* of scientific and technological developments are always unforeseeable, he cannot in good faith allege that the time has come when all their *benefits* are foreseeable. Moreover, Cavalieri's competence to discuss, not ethics, but modern DNA research is put into question by his failure to mention the amazing advances that recombinant DNA techniques have brought to our understanding of the molecular organization of genetic structures in the past three or four years. An author of a book on recombinant DNA that appeared in 1981 who does not mention the discoveries of the fragmentation of eukaryotic genes and the mechanism of generating the diversity of antibody specificity, neither of which could have been made without the use of recombinant DNA methods, commands just about as little credence among biologists as one who, in the 1960s, would have failed to mention the discovery of the genetic code.

Gunther S. Stent is Chairman of the Department of Molecular Biology and Director of the Virus Laboratory at the University of California, Berkeley.

A haunted house of cards

D.R. Newth

A New Science of Life: The Hypothesis of Formative Causation. By Rupert Sheldrake. Pp.229. ISBN 0-85634-115-0. (Blond & Briggs: 1981.) £12.50. To be published in the US in January 1982 by Tarcher, Los Angeles.

THE title of this book is misleadingly modest. The author is not content to propose only a new science of life, for he reassesses many features of the real world that have been revealed by natural science, and proposes that there exists a great conservative principle making itself felt as much, or more, by sub-atomic particles as in developing embryos or in the behaviour of human beings. The principle is that what happens, or has happened, can exert an influence that is without decrement in space or time upon future events of a similar kind. This influence acts to promote a repetition of what has gone before. The degree of similarity qualifying a living organism to respond to these persuasive messages appears to be

conspecificity. Not all decisions or events, however, are susceptible to the principle of "formative causation".

The immediate recipient of the messages is a "morphogenetic field" which guides formal change in its associated "morphogenetic germ" until its prescriptions have been met and the "morphic unit" is finally co-extensive with the field. The morphogenetic field blends the experience of all previous similar morphic units by a process of "morphic resonance". Neither morphic resonance nor the obedience of the morphogenetic germ to the dictates of its morphogenetic field involve exchanges of matter or energy.

This, I understand it, is the burden of Dr Sheldrake's argument.

It is, of course, brave to expound in little more than 200 pages so revolutionary a denial of everything that empirical science has made seem probable. Nor should we deny some leniency to the holders of really way-out ideas. They lack the support of an established terminology, and the com-

forting background of assumptions held in common with their readers. But they should at least try to be clear, at whatever cost to their credibility.

Dr Sheldrake writes as Mrs Bloom daydreamed, with no one theme rigorously explored before it sets off another which before resolution gives way to something else again. It would be unkind to suggest that this is a device for escaping from difficulties, but even readers who are wholly unsympathetic might welcome a clearer view of the author's position. For example, in discussing the limitations of morphic resonance he assumes that while past events can be effective now, future events cannot. While conceding that it is logically conceivable that they might be, he excludes the future on the ground of simplicity and remarks severely that "only if there were persuasive empirical evidence for a physical influence from future morphic events would it become necessary to take this possibility seriously". Apart from the ambiguity of introducing *physical* influences into a discussion of extra-physical phenomena, one is left wondering why the same severity is not applied to the past.

Indeed, Dr Sheldrake does believe that his ideas are capable of receiving support from experiment, but his proposals for experiments are curiously tentative and unsatisfactory. Thus

...if thousands of rats were trained to perform a new task in a laboratory in London, similar rats should learn to carry out the same task more quickly in laboratories everywhere else. If the speed of learning of rats in another laboratory, say in New York, were to be measured before and after the rats in London were trained, the rats tested on the second occasion should learn more quickly than those tested on the first.

Well, yes, but so they should without the London intervention, and any quantitative predictions in the operation of this hypothetical principle are so wholly arbitrary that the design of such experiments would be difficult indeed. Dr Sheldrake concedes this in his rather casual

suggestions for a handful of investigations in each of which he describes a possible result *supporting* formative causation, but the opposite result is inconclusive. It would be a help if he could offer us predictions the failure of which would end the matter.

Anyone tempted to take formative causation or morphic resonance seriously should ask themselves why. A world haunted by messages from the past, some, like those from morphic units of extinct species, destined to vibrate eternally and in vain while seeking a morphic germ with which to resonate, may have a poetic appeal. Unfortunately it may also appeal to a perverse fear of scientific understanding. Dr Sheldrake explains early in the book

that while some outstanding biological problems are difficult, others are, in principle, insoluble — for example, those associated with evolution and with the origin of life. Neither, as it happens, is suitable for the operation of formative causation, since they are creative and unique rather than repetitive. But by the end of his exposition one reader had the distinct impression that intrinsic insolubility had its own attractions for him and that the hypothesis of formative causation was his contribution to a happy state of confusion. □

D.R. Newth is Regius Professor of Zoology at the University of Glasgow.

Selling newspapers and selling science

Eric Ashby

Reflections on Science and the Media. By June Goodfield. Pp.128. ISBN 0-87168-252-4. (American Association for the Advancement of Science: 1981.) \$9.

"JULES de Goncourt once wrote that . . . the newspaper bore the same relationship to a book as a whore did to a decent woman". A verdict, as June Goodfield says, "too harsh by far"; but as a caricature of the way some of the mass media deal with science it has an uncomfortable relevance. A news item is a one-night affair unless it attracts enough readers or the TV ratings to justify a follow up. As soon as the issue no longer stimulates the reader or the viewer it is dropped. Never mind that the issue is important, still unresolved and ought to be kept before the public: out it goes to make room for something more newsworthy. Of course there are honourable exceptions to this generalization, but as a rule news keeps no better than fish; indeed less well than fish, for fish can be put in cold store and still eaten with relish. News that has been put in store is worthless.

This is one of the reasons for the mutual suspicion between scientists and journalists. They work on different time-scales. The scientist who publishes half-baked findings loses the respect of his peers. The journalist who fails to publish his findings promptly, however half-baked they are, loses his job. And on the journey from the laboratory to the news-stand the information may get horribly distorted. The interview between journalist and scientist may have lasted an hour; the journalist has to chip away the reservations and complexities so that he can fit the story into half a column; the sub-editor (the worst culprit of all) slices chunks out of the journalist's copy and adds a sensational headline which must often sicken the journalist as well as infuriate the scientist who in good faith has explained his work.

And the outcome: a wider alienation between science and the media.

This didn't matter in the days before the public became the patrons of science. It would not matter today if everyone read the *New Scientist* or the science correspondents in the quality newspapers, or even watched science programmes on the BBC. But they don't, and they pay taxes some of which support science. What should they be told about science?

In the United States the presentation of science on TV is much less satisfactory than it is in Britain, and science in the mass-media newspapers is no better reported than it is in Britain. The only science that is "sold" to the public is likely to be scandalous (for example the thalidomide affair) or open to ominous speculations (genetic engineering) or fashionable (pollution, in the 1970s). What is urgently needed is a much better public understanding of what science is about, how it is done and what consequences it has for society. These are difficult matters to put across and there's no money to reward those who try to do it.

It was, therefore, an excellent idea for the American Association for the Advancement of Science to commission an essay on science and the media, and a brilliant choice to offer the commission to June Goodfield, who already has an international reputation for her interpretation of science to the so-called lay reader. With first hand experience in the two professions of journalism and science and a sympathetic understanding of the constraints under which both these professions work, she has offered a clear — and in places refreshingly provocative — analysis of the "uneasy relationship" (as she calls it) between the two professions.

She rejects the view (still held, alas! by some scientists) that the great bingo-playing, football pools, top-of-the-pops majority don't need to be told about



Rupert Sheldrake — contribution to a happy state of confusion?

Lindy Guinness

science and wouldn't understand it anyway. They do understand the science stories that do get into the mass media: if this were not so, the science stories would not appear there at all. But this does not mean that science reporting must be sensational. Members of Mechanics' Institutes in the nineteenth century responded with enthusiasm to the journalistic essays of Faraday. Readers of the tabloid press were enthusiastic about science reporting by J.B.S. Haldane in the 1920s. So, there is a strong case for science journalism at this very popular level to be accurate, enlightening and responsible. What constraints stand in the way?

For the mass circulation newspapers the constraints are that the news item must arouse immediate interest, it must be grasped at first reading, and it must have an element of novelty. (How close to the bone was the analogy of Jules de Goncourt!) If papers don't sell they go out of business. Released from these three constraints they would not sell.

For television news, as contrasted with sustained scientific programmes such as *The Ascent of Man* and *Life on Earth*, there are similar constraints. A Select Committee report (on hazardous wastes, for instance) is published on a Tuesday. It is, let us say, 150 pages long. On Tuesday evening it will have to be reported "on the box", with a verdict on its merits or (preferably) its deficiencies, mustered that afternoon over the telephone. In Britain some of the sustained programmes are splendid. This is possible (as June Goodfield explains) because the producer is "totally responsible for the content and impact of the work". He doesn't have someone else in the hierarchy breathing down his neck all the time. In America it is otherwise; there "the long arm of sponsorship" reaches down even to the details of the production. Even public television, where there have been some successes, seems constrained to plug the wonders of science rather than the experience of doing science and the effects science is having on the way people live.

The scientist, too, works under constraints that block his contacts with the public. His peers, higher in the pecking order of distinction, are breathing down his neck: too much (or, just as bad, too successful) popularization, and the whisper "not altogether sound, you know" echoes in the academic groves. News is enlivened by human interest, so the media like a little autobiography to be brought into a science story (hence the success of James Watson's *The Double Helix*). But it is the aim of scientists at work to be self-effacing; they never publish their false starts, their failures, their own reactions to the research they do: all these are filtered out before the paper is sent to the learned journal to be published. The chief constraint is the necessity imposed by the conventions of scientific research — not to reach premature conclusions, not to

advance to a position from which you may one day have to retreat, and never, never, in reporting research, to extrapolate beyond your data to broad speculations. If your research does have social consequences, discussion of these has to be put into different journals addressed to a different readership. This is one of the difficulties science reporters have to contend with.

June Goodfield illustrates the difficulties in the way of bringing journalists and scientists on to the same wavelength by four examples. There was the scramble of reporters to make a sensation out of the affair of Summerlin's painted mouse. In their haste to get a story out, all but one of them got the story wrong. Only one journalist, Gail McBride of the *Journal of the American Medical Association*, took the trouble to understand the whole story, and (of course) by the time she published, four months after the event, it was no longer news. Then there was the worldwide, and at times hysterical, publicity following the Asilomar conference on recombinant DNA. There was an even more hysterical exhibition over Rorvik's false claim about a cloned man, exposing the venality of a publisher who contrived to create a best-seller out of the phoney book. And there was the example of investigative journalism at its best: the sustained campaign to expose the cover-up over thalidomide.

With great skill June Goodfield attempts a summing-up. Both scientist and journalist begin on common ground: it is their business to discover and to publish the truth. Neither profession has an explicit code of ethics, nor a controlling body which (like the General Medical Council) can deprive a practitioner of his right to practise. In science, peer opinion provides a crude, but on the whole effective, mode of control. Shoddy work is not condemned in bitchy articles, such as Leavis wrote about Snow; it simply sinks without trace.

In journalism the implicit code of ethics is weakened by a pervading hypocrisy. It is a scoop to publish a secret government document illegally obtained; it is also a scoop to expose someone outside the profession who has obtained a secret document for his own ends. A contractor who bribes a politician is fair game for publicity, but not a journalist who bribes a witness. June Goodfield wants journalists to tighten their code of ethics but she would like them also to assume some responsibility to act as critics of the ethical implications of science. The need for this arises because scientists do not have a cloud of critics hovering round them, as novelists and dramatists have, and they deliberately dissociate their work from its ethical overtones.

As for the scientists, she wants them to take the trouble to sympathize with the constraints under which journalists have to work, to be less arrogant and more co-

operative, to realize that journalists are an essential channel of communication between themselves and the public on whom they depend for a livelihood. She wants devices for disseminating information in suitable form to the media. She wants the interpretation and communication of science to be taken more seriously as disciplines in universities, so that a student could find training for science-writing.

Her main suggestion is that there should be critics in science who play roles like those played by critics in music, literature and the arts, critics "in the accepted, old-fashioned meaning of the term". This is the one point in June Goodfield's essay with which I disagree; for two reasons. First, the achievements of science are published normally as papers in journals, not as books. (For books there is a mild critical apparatus already, e.g. in the review columns of *Nature* and other science magazines.) Second, the scientific content of research papers is effectively criticized by the use made of the papers by other scientists. Research of high quality is quoted. Research of poor quality is disregarded. So I see no merit in having professional science critics. If all critics were like Walter Lippmann or Edmund Wilson or Donald Tovey, that would be fine. But critics now abound like carrion flies, swarming over the work of people engaged in the desperately difficult professions of literature and art, dismissing, with a patronizing drawl, such as one hears on some radio programmes, creative work they would be quite incapable of doing themselves. God preserve us from critics like that in science. Nor will they be needed while there are scientists about who have June Goodfield's brilliant capacity to work at the interface between science and the humanities. □

Lord Ashby is Chancellor of Queen's University, Belfast, and a Fellow of Clare College, Cambridge.

The measure of man

P.B. Medawar

A History of the Study of Human Growth. By J.M. Tanner. Pp.499. ISBN 0-521-22488-8. (Cambridge University Press: 1981.) £30, \$69.

PROFESSOR Tanner has made important contributions to the practice and methodology of anthropometry; one thinks especially of his studies of secular changes in human growth rates and in landmarks such as age of onset of sexual maturity in the two sexes. He is well known also for his advocacy of the cohort method in the analysis of human growth (the "longitudinal" method as opposed to the more familiar "cross-sectional" method

which has the disadvantage that curves of growth tend always to be confused by curves of distribution).

It is not usual for practitioners of a science to write of its history, but if it comes off, as it does here, the result is a triumph. Tanner could hardly do otherwise than begin with the voluminous and in the main tiresome works by or attributed to Aristotle: instead of calling attention to his more egregious and least easily explicable blunders, such as the belief that human semen is infertile until the age of 21, Tanner makes the best of Aristotle by finding grounds for the neat and convincing inference that "in 350 BC children were maturing at approximately the same rate as now".

Among Tanner's most interesting passages are those that deal with the hebdomadal tradition: the number-magic that found expression in the belief that the body is divided into seven parts and the life of man into seven stages each seven years long.

The mystique attached to the seven-fold system makes reliance on the truth of any actual age impossible however; both at the time and for centuries later there is a tendency for all ages to be rounded to the nearest hebdomadal number.

Tanner is a learned and widely read man, and his book is full of fascinating historical and sociological insights:

... the growth of children of the manual labouring classes in England in the 1830s, and even the 1870s, was still more depressed than that of the poorer groups in some of the underdeveloped countries nowadays ... we should not be too surprised. Indeed children of slaves in the plantations of the southern states of America at this time ... were taller (by some 2 to 5 cm) than contemporary children of manual labourers in England (although nowadays the heights of children of European and of African descent living under similar economic circumstances are almost identical).

Tanner devotes some amusing paragraphs to passages from J.J. Virey ("that would have done credit to Baden Powell") professing to demonstrate the debilitating effects of masturbation. J.J. Virey (1775–1846) was a pharmacist who contributed to the *Dictionnaire des Sciences Médicales*.

Although the book is mainly about human growth, Tanner casts a wider net and manages to make mention of D'Arcy Thompson, who had little to say about human growth. As an admirer of D'Arcy's, I can vouch that Tanner's placing and appraisal of him are exactly right — "a late flower of the Renaissance" who wrote superlative prose.

This is an excellent book which may be read with advantage by all biologists interested in the history of ideas — and should certainly be read by sociologists and social historians as well. □

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Education in science, science in education

Nevill Mott

Science in Schools: Which Way Now? By Richard Ingle and Arthur Jennings. Pp.185. ISBN pbk 0-85473-100-8. (University of London Institute of Education/NFER-Nelson: 1981.) £5.30.

THE authors of this book give an account of what has been happening in science education in the UK and of what, in their opinion, ought to happen now. One of them graduated in physical sciences, the other in biology; both had considerable experience of school teaching before moving into the field of teacher training and educational research. The emphasis of their book is on "science for all" and it gives as clear a discussion as any I have seen of the objectives to be achieved by giving all children, up to the age of 16, considerable time for science. What the authors discuss rather little, in that they do not present it as a separate problem, are the needs of that minority who after further education are going to make use of their science, as engineers, technicians, research scientists and doctors.

The rise of general science in the interests of science for all, and its subsequent decline up to the time of the change to comprehensive education, is described here, as it is perhaps more fully in the chapter "The General Science Movement" in E.W. Jenkins's book *From Armstrong to Nuffield* (John Murray, 1979). In the years between the two wars, Ingle and Jennings say that the move towards general science was based on the notion that science should be for everyone, not just for the embryonic professional scientists (which presumably includes engineers, doctors and others), and that it should form an essential part of the general education of all young people. But in practice, they add, general science was found to be "a scrappy mixture of physics, chemistry and biology". Certainly, in the immediate pre- and post-war periods it enjoyed little prestige as a university subject, in comparison with the specialist honours degrees. Moreover in the post-war period, policy-makers, conscious of the role of science in the war and of the perceived need for qualified scientists and engineers (QSEs) in industry, had little use for general science. Two authorities, quoted by Jenkins (p.99) wrote that

An improvement in ... school science teaching is a requirement for the continued existence of this country as a leading scientific and industrial nation. As a first step in this direction general science should be abandoned.

Ingle and Jennings report that in the 1950s, in independent and grammar schools, general science was declining fast and two or three specialist O-levels were the norm. However, in the secondary modern schools, they say, teacher training colleges serving them were sufficiently independent

from universities to help teachers make the science more child-centred and less academic than in grammar schools. Unfortunately these teachers were rarely encouraged to publish their methods, "so that their experience and wisdom died with them".

A second chapter deals with "the curriculum development era", starting in 1960, and particularly the Nuffield Science Teaching Project, beginning in 1961–1962. This aimed to produce material in the three separate sciences, initially in the age group 11–16, for children in the selective grammar schools, and equally suitable for both future science specialists and others. In all three projects it was the aim that children would learn science largely through experimental enquiry, with the guidance and support of the teacher. The reception of Nuffield in the schools is described, as is its influence even in schools where the whole package was not accepted. Two criticisms of the original Nuffield scheme have been that the work was very demanding, even for the more able pupils, and that neither the O-level nor A-level schemes went far in illustrating the social relevance of science. Later projects for the less able child are described, including Nuffield Science 13–16 (now being published), the Association for Science Education's (ASE) project for "Less Academically Motivated Pupils" (LAMP), and also the much more demanding Schools Council's Integrated Science Project (SCISP), which with a time-table allocation equivalent to that for two O-levels brings together the three sciences with time for ample attention to be paid to their social aspects. Also described is the Schools Council's Project Technology, which had the aim of helping pupils to understand the importance of engineering in our way of life. In spite of the expenditure of £300,000, this project, they say, has had little impact; perhaps this is because science teachers teach best what they know best, and very few science teachers have been trained as engineers. In this context, the authors include an apposite quotation from B. Prescott:

Perhaps one of the greatest weaknesses of science teaching is that it is science teachers who do it — science teachers who have been initiated into the profession by science teachers and they teach courses written by scientists and science teachers.

But if this is a weakness, how is it to be corrected?

In chapters on aims and ideals in science education, and on hopes for the future, Ingle and Jennings identify themselves with the swing back towards general science and science for all, and away from the objective of producing QSEs, a movement which has undoubtedly taken place in the last decade. Reasons for this

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

Physics for sixth-formers — in the 1980s will they receive the grounding they need?

are perhaps the introduction of comprehensive schools, the unfavourable image that science and technology has sometimes presented and a widespread reaction against the so-called elitism of conventional scientific education. An extreme example of this reaction was the issue by the ASE of its discussion document "Alternatives for Science Education" (1979) which two years ago sent a shock wave of dissent through more conservative circles.

In this document it was claimed that science education as it is now is elitist, designed for the minority intending to make a career in science and against the interests of the majority. Alternatives were suggested, some of which seemed to propose teaching more about the role of science in the modern world than the practice of science itself. The ASE's most recent document, "Education through Science", issued in August 1981, puts forward a more moderate policy for the future which does not differ much from the proposals in the book under review, and which indeed carries widespread support. It is proposed that in all schools for children between 11 and 16, one-sixth of school time should be spent on science — this would correspond to the time spent on two O-levels — and that integrated courses including physics, chemistry and biology, tit-bits of other sciences and coverage of social implications would be devised. This, it is claimed, would avoid irrevocable choices at 13, which so often cut children and particularly girls off from careers in science and its applications. Also it would avoid the lack of balance between science and the humanities which the study of three separate science subjects is said to involve.

Thus science education, as mapped out in this book, should be intended for all children. Rather than summarizing the aims set forth by the authors, the flavour of their argument may be given by the following quotation from a CSE project report which they include in the book:

My project worked very well and I'm pleased because (i) I got alcohol from paper which I thought was never possible, (ii) because I used some new equipment which I've never herd of let alone worked with. Another thing I was pleased about was there was lots of experiments and if there was anything I wanted to know there was

book's at my finger tips so there weren't any time lost. If I had a lot more time what I would like to make is a lot more alcohol and do lots of flame tests because I only made about 1cm³ of pure alcohol. So I could not do much, I would also like to find how much yeast is necessary to ferment it properly yet let the alcohol burn properly. I would also like to know if it was the yeast that stopped it burning. I would also like to learn how to control the heat when distilling because that a mistake I made.

Curiosity, ability to think and to form ideas of what science and technology are about are to be emphasized. The authors recognize that "there are many young people who will leave school to seek employment in some field of science and technology, and that these will need a more extensive knowledge of science". Reference is made to "the more demanding courses that *may* be necessary to engage their minds and prepare them for sixth form studies". The italics are mine. Little discussion is devoted to the vexed question of setting or streaming for these more demanding classes. The authors give the impression that, although they realize that setting in science subjects (or avoidance of science by the less talented) is almost universal, at any rate from 14 to 16, they hope that mixed ability teaching will spread. But this book does at least recognize the needs of the talented.

Two years ago the Education Committee of the Royal Society issued a discussion paper entitled "Science and the Organization of Schools in England; Implications for the Needs of Talented Children". Here it was taken for granted that setting for science and mathematics was in the interests of talented children, that they needed to be with children of like ability and to make progress at their own rate. The fear was expressed that in small comprehensive schools, particularly if falling rolls should make them still smaller, there would not be enough children to form an O-level class. It also defended the retention of three O-levels together with a choice of subject, among other reasons because teachers can teach best what they know thoroughly. It is true that almost any reform is bad if it does not increase the teacher's confidence in his mastery of his subject; for this reason Ingle and Jennings rightly stress the need for in-service training, preferably school based.

If school education goes the way recommended by Ingle and Jennings, we can envisage a future as follows. All children will spend one-sixth of their time on science up to the age of 16. There will be a common examination system, unifying CSE and O-level, but separate questions or even papers of appropriate difficulty may be set. The separate teaching of physics and the other subjects may disappear, except perhaps in the independent sector. There will be a common core; the lower ability groups will not have vague talk about science fobbed off on them but will be exposed to some real science. Ideas on the teaching of the less talented will develop, and some success is expected. Setting, however, is likely to remain. The experience with SCISP shows that talented children who have done the equivalent of two O-levels do not have difficulty with A-levels as they now are. Whether more science teachers able and willing to teach all three sciences will be found, only the future will show.

We have here a way forward which, I believe, may well be in the interests of the average child and also of the more talented child who does not want to specialize in science. But for future scientists, I have doubts. Probably a wider education, cutting down in the time spent on science up to the age of 16, will not do them any harm. On the other hand, if they are held back, and not allowed to progress as fast as they can, they may become disillusioned and even give up the subject. How much do we want to keep the most talented back, in the interests of the majority, or of general education or for any other reason?

If the authors of this book do not see this as a major problem, they have much of interest to say on many other matters. One is the need for collaboration between the teachers of science and of mathematics; another, perhaps more original, is the help that historians ought to give in teaching the history of science. Another is the value of education in science towards learning to express oneself clearly. Finally, the authors quote Richard Peters as writing (in 1972) that "our state of ignorance with regard to teaching is comparable to that of the Greeks with regard to medicine or meteorology". Ingle and Jennings end their book by expressing the hope that systematic school-based research will hasten the day when science teaching, while remaining an art, will become more of a science. And as a consequence, they hope, as we all must, "that the promotion of teachers might then begin to depend less on confidential references and more on soundly based competencies". □

Sir Nevill Mott was Cavendish Professor of Physics until his retirement. He was a member of the Crowther Committee on education from 16 to 18, and has chaired various advisory committees for the Ministry of Education and for the Nuffield School Science Project. He is now a member of the Royal Society's Education Committee.

Camera Press

The eighteenth-century generation game

Christopher Lawrence

Matter, Life and Generation: Eighteenth-century Embryology and the Haller-Wolff Debate. By Shirley A. Roe. Pp.214. ISBN 0-521-23540-5. (Cambridge University Press: 1981.) £16, \$32.50.

AT FIRST sight the eighteenth-century debate on the nature of generation and embryological development might appear to have been a parochial affair. The path from fertilization to birth, however, was by no means a simple scientific conundrum calling for a straightforward empirical enquiry. As Professor Roe displays so clearly in this excellent book, generation was a hinge on which turned alternative cosmologies. Different theories of development brought into conflict incommensurable universes. Professor Roe has therefore used this particular study as a case history to illustrate some more general philosophical points about the nature of scientific enquiry and explanation.

In the eighteenth century there were two possible views on generation which were scientifically respectable. Preformationists held that embryos pre-existed in either the semen or the egg and these embryos in turn, like a nest of dolls, contained intact the next generation in their germinal material, and so on. This theory, first fully articulated by Malebranche in 1674, had considerable advantages over its rivals. The scientific revolution had virtually swept the intellectual field by the late seventeenth century. It left behind only matter, motion and — after Newton — force as the fundamental explanatory principles in the cosmos. Preformationism therefore explained the puzzle of why it was that the embryo developed in the way it did, rather than crediting the possibility that matter in motion could somehow give rise to organized material.

This latter eventuality was embraced by the epigenesists, who held that the embryo developed form and parts from where there

had been neither form nor parts before. The most famous epigenesists of the eighteenth century were Maupertuis, Buffon and Needham, and in the world of belles-lettres the philosopher Denis Diderot. All of these thinkers circumvented the problem of formal development by postulating that matter was innately active and not the passive servant of other forces. The preformation-epigenesis dichotomy therefore was not a simple scientific schism. Rather, on the one hand lay the divinely formed embryo, special creation, a meaningful universe, and thus a Christian cosmology and salvation. With epigenetic development lay chance, purposelessness, Lucretianism and extinction.

In the middle of the eighteenth century this debate was rekindled by the pious, Newtonian, Professor of Anatomy at Gottingen, Albrecht von Haller and the rationalist, upstart physician, Caspar Friedrich Wolff. Haller espoused preformationism and Wolff epigenesis, and for ten years they discussed the issue in print and in private correspondence. Two factors make the debate particularly interesting. First, they both conducted a great deal of detailed empirical research on the development of the hen's egg, attempting to discover or refute whether the chicken came first so to speak. The debate thus turned on complex technical questions such as the appearance of the heart, the gut membranes or the yolk sac vessels. Second, Wolff was no ranting atheist. Rather, he too was a deeply pious Christian, but one who had begun with his feet in quite different metaphysical starting blocks to those of Haller. For Wolff, the laws of motion observed by matter had been created by God in the first place. Thus, epigenetic development was, in a way, preformationism one stage back.

Professor Roe unfurls this dialogue, or rather these two monologues, and shows clearly that, given the metaphysical corners of the protagonists, neither was going to get near enough to strike a blow. Where Wolff saw a heart developing and new bits forming, Haller saw a previously transparent structure becoming denser, coloured and demarcated from its surroundings. Professor Roe reveals these aspects of the debate with faultless precision founded on superb scholarship.

What is disappointing, however, is that she stops short at either end of the argument. At the observational end she offers no discussion as to whether Haller and Wolff were interpreting differently the same data or whether they were actually seeing the world differently. Professor Roe never says whether Haller ever disagreed with Wolff's embryological drawings and denied that they represented reality, or whether Haller only disputed the meaning

of agreed observations. Neither is it clear whether Haller produced any drawings of what he saw. At the metaphysical end of the argument, Professor Roe seems to suggest her task is over when she has related a scientific debate to more general metaphysical principles. Having shown that the world rests on the back of an elephant, she neither asks if the elephant itself rests on anything or, if not, shows why her explanation of the Haller-Wolff debate might be sufficient once the metaphysics have been invoked. The epigenesis-preformationism debate is therefore still a somewhat circumscribed area in eighteenth-century science. After this book, however, historians will need to perambulate a much extended perimeter fence. □

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Battle over bacteria

G.D. Heathcote

The Fischer-Smith Controversy: Are There Bacterial Diseases of Plants? Phytopathological Classic No.13. Translated and prepared by C. Lee Campbell. Pp.65. ISBN 0-89054-014-4. (American Phytopathological Society, 3340 Pilot Knob Rd, St Paul, Minnesota: 1981.) \$8.50.

PROBABLY few plant pathologists will make the time to read this pamphlet, which consists of little more than seven review papers published in Germany between 1897 and 1901, but the American Phytopathological Society did well to publish it. Perhaps they did so because it has a plot which could not fail to appeal to the American spirit. It tells how Erwin Smith, originally a poor farm boy from Michigan, battled (with words only of course) against the academic might of the classically trained Alfred Fischer, once an unsalaried lecturer in botany at the University of Leipzig, at the time when plant pathology was almost a German science.

The debate as to whether or not bacteria can be the direct cause of disease in plants stimulated the two protagonists into making bitter and personal attacks against each other. Smith's statement regarding part of one of Fischer's lectures: "It is seldom in a genuinely scientific book that one finds so many unwarranted assumptions and serious misstatements in the space of a single page . . ." would undoubtedly have infuriated Fischer, and attacking Smith he wrote: "... after experiments of that kind . . . no one will think badly of me that I had not sought further statements in the American

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Chicken development — detail from Fabricius's *De Formatione Ovi et Pulli* (*Opera Physica Anatomica*, 1625).

By courtesy of the Wellcome Trust

literature when I wrote my lecture”.

Fischer was convinced that bacteria are only saprophytic upon tissues already broken down and that they cannot penetrate undamaged cells. Smith quoted experiments showing how bacteria can dissolve cell walls and that they can enter undamaged tissues, for example pear blight bacteria can penetrate through nectaries. In the end nobody won as such. Smith died in 1927 after a long and distinguished career, and although Fischer eventually suffered from depression and committed suicide in 1913 his professional stature was not diminished by the controversy.

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

Erwin Smith, farm boy turned plant pathologist. In 1899 he wrote of Fischer “. . . he garbles and misrepresents, charging other men with being stupid blunderers . . .”.

Nonetheless, the debate proved to be a significant event in plant pathology. Smith's view became accepted, and plant pathologists began to work seriously on bacterial diseases. Today between 180 and 200 species of plant pathogenic bacteria are recognized, causing serious economic loss throughout the world. They are unable to penetrate the plant cuticle and many require wounds to gain entry into the host plant but some enter through natural openings. Many are windblown or disseminated by splashing water, and at least 60 species can be carried by insects, for example fire blight of apples and related species is carried by honey bees.

The statements some of us make today are usually shorter but they are no more reasonable than those made by our predecessors. I can well remember the disbelief when it was first suggested that nematodes can carry virus diseases, and some of the diseases I thought to be caused by the viruses have been shown to be caused by mycoplasma-like organisms. Like so many controversies of the past, the Fischer-Smith debate repeats the lesson that in plant pathology, as in all of science, dogmatism is dangerous. □

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Test tube to womb: ethics and politics

R.V. Short

From Chance to Purpose: An Appraisal of External Human Fertilization. By Clifford Grobstein. Pp.207. ISBN 0-201-04585-0. (Addison-Wesley: 1981.) \$17.50, £11.50.

IN THIS book Dr Grobstein, Professor of Biological Science and Public Policy at the University of California, San Diego, seeks to describe for the general reader the technical procedures involved in human *in vitro* fertilization, and the social and political implications of this work. We are told that Dr Grobstein is internationally known for his research in developmental biology, and so we are entitled to expect a good read, and a penetrating analysis of present developments and future prospects.

The book turns out to be little more than an annotated commentary on the report of the US Ethics Advisory Board on Research Involving Human In Vitro Fertilization and Embryo Transfer, which was published in 1979. Fortunately this report is reprinted as an appendix, and for those not already familiar with it, it will form by far the most interesting part of Grobstein's book. Joseph Califano, the former Secretary of Health, Education and Welfare in the Carter administration, deserves considerable credit for setting up the Ethics Advisory Board, alas now disbanded, and charging such a distinguished group of scientists, lawyers, theologians, clinicians, ethicists and administrators with an in-depth investigation of the whole subject of *in vitro* fertilization. The way the Board went about this task was commendable. They commissioned manuscripts from leading experts known to have views on the matter, and held public hearings around the United States, with live radio and television coverage, to which anyone could give testimony, and at which the experts were cross-questioned by the Board. All the written evidence was then published, together with the incisive, common-sense judgements of the Board, who must have been greatly indebted to their chairman, a lawyer, James C. Gaither, for producing a consensus report from a Board that itself embraced such widely divergent views. The conclusions were neither remarkable nor controversial. The human embryo is entitled to profound respect, but this does not necessarily encompass the full legal and moral rights attributed to an adult individual. Therefore, a broad prohibition of research involving human *in vitro* fertilization is neither justified nor wise. Federal support for such work would be ethically acceptable, and there is a need for more research in order to assess the risks to mother and offspring.

The Board managed to steer a course between the Scylla of those such as the President of the Massachusetts Council of

Rabbis, who thundered that “Further *in vitro* experimentation could tend to eliminate the need for the human family and turn humanity into a zoo of fertilized and fertilizing animals”, and the Charybdis of the brothers Seed (*sic*) who offered to buy fertilized eggs flushed from the uteri of women donors, and transfer them to the uteri of infertile recipients — at a price. Nevertheless, the publication of the Board's findings in the Federal Register on June 19th 1979 produced a storm of written protest from, one suspects, the Right to Life group. Secretary Califano took no action on the Report's recommendations, and shortly thereafter resigned. The Ethics Advisory Board was then disbanded because Congress established a new “President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research”, that does not seem to have addressed itself to the problem, and America changed Presidents.

Since that time, nothing more has been heard of the Board's report. It seems to have sunk without trace, presumably too hot for a right-wing administration to handle. But thereby went an honest attempt to reach a consensus view by public debate of a contentious issue, and much time and money was wasted in the process. It is sobering for scientists to realize that even if an issue is scientifically, socially and ethically acceptable, it will receive no governmental support unless it is politically expedient. But Everyman will have the last say; new clinics are opening up around the world, and the number of successful births following *in vitro* fertilization is now into the teens. Even the President of the United States cannot halt such progress, although the paucity of governmental funding for the back-up research that is so urgently needed can significantly delay it. The success rate of the procedure is still very low, and research could surely improve it to the point where we might expect a 25 per cent chance of pregnancy following embryo transfer, which is the probability that a fertile woman has of conceiving in an ordinary menstrual cycle.

But all of these comments relate to the appendix. What of the book itself? It has little to add that is new, much that could have been discussed is missing, and several statements are factually incorrect. As for its good points, it is sensible to suggest that we should re-name *in vitro* fertilization “external fertilization”, a term that is infinitely preferable to “test-tube baby”, which has alas probably come to stay. Grobstein also has an interesting chapter on “Becoming a Person”, in which he propounds the common-sense view that “neither life nor the human quality begins in any generation. Human life, like that of all species, descends without break from

generation to generation. It waxes and wanes in complexity but never begins *de novo*". But he has an ungainly style of writing: talking of human attributes, he says "As a group they span the biological, behavioral, and social realms, constituting a kind of slope between animal and human states along which our species has moved evolutionarily and continues to cycle generationally".

Although there is much discussion about "circumventing the oviduct", a valuable opportunity is missed by failing to compare this with "circumventing the penis"; the ethics of artificial insemination, whether by donor or husband's semen, have been widely discussed in recent decades. On the technical side, it is disappointing to find no mention of ultrasound, which is now widely used as a non-invasive way of monitoring follicular development. There is no discussion of interspecific fertilization, and yet use of denuded hamster oocytes to bioassay the fertilizing capacity and examine the karyotype of human spermatozoa has been an exciting

recent technical advance, one which still seems to send an ethical shudder through the World Health Organization.

As for the mistakes, how unfortunate to depict luteinizing hormone as a secretory product of the posterior pituitary gland; how naive to believe that infertility in men is often *the result* of a low sperm count, so that merely increasing sperm density by centrifuging a semen sample will increase fertility. Recent evidence from hamster oocyte preparations shows quite clearly that oligospermic men are infertile because of some basic defect that results in the ejaculation of small numbers of spermatozoa each of which has a significantly reduced fertilizing potential; concentrating the ejaculate is therefore a waste of time. And Edwards and Steptoe, who after all pioneered this whole field, will be interested to hear that the work was done at Oldham Hospital in Cambridge, England! Not a book to recommend. □

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Lessons for twentieth-century nutritionists

John Rivers

Nutrition and Nutritional Diseases: The Evolution of Concepts. By Karl Y. Guggenheim. Pp.378. ISBN 0-669-03950-0. (Collamore Press, Massachusetts: 1981.) \$21.95.

ALTHOUGH this is an important book, it must be admitted at the outset that it is not a historian's history. Professional historians of science will no doubt be irritated by the brevity with which many subjects are necessarily treated and by the occasional lapses that suggest historical naivety (for example, calling Boyle's school "Eaton", or seeming to equate Pereira's training as an apothecary with pharmacy not medicine).

But whatever its reception by historians, nutritionists will I hope buy and read this book, for it is an important history of their discipline and their profession, and one that they should study. It is all the more valuable because Professor Guggenheim is not a trained historian, but a nutritionist who, after a lifetime of research into the practical problems of nutrition, has produced this scholarly work in his retirement.

The discipline of nutrition is an uneasy coalition. Its scientific roots are in aspects of physiology which had their heyday in the nineteenth and the first half of the twentieth centuries. Its justification is a wide spectrum of unresolved practical problems, from tooth decay to the world food problem. And nutritionists, it must be admitted, are people who, by and large, fail either to revive the science or solve the

problems to which it is addressed. As long as it is possible to imagine that, even if the next experiment won't save the starving masses at a stroke, it is a step in that direction, then there is an excuse for surfing along on the wave-front of the present. But as it increasingly appears that poverty not protein is the key to malnutrition, and that tooth decay can only be cured by drawing the teeth of the confectionery industry, the nutritionist increasingly needs to take stock and decide whether he is really necessary.

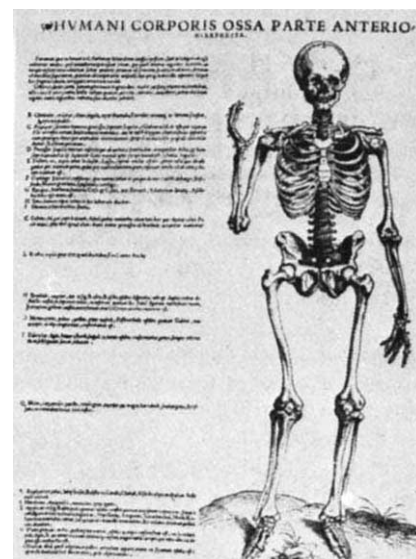
Individual action is of course irrelevant. What is needed is a dialogue within and beyond the profession about the extent to which nutritional science should be coupled to practical policy. Such a discussion would need to be guided by a coherent view of the past, and without the historian's spotlight can probably never begin. It is self-evident that such historical studies on nutrition as exist at present have not had any such catalytic role — not surprisingly, for where they are not social histories of diet, they are catalogues of achievements of the great and famous.

The significance of Professor Guggenheim's new book is that it is free of that tradition and hopefully will have a powerful impact. He does not merely re-tell the story of the development of the science of nutrition, but, more than any other work on the subject, he studies its growth mechanisms. His avowed aim is contained in the subtitle — he tries to trace "the evolution of concepts". He does so with great fluency, and in a way that is

realistic, in that it sees the concept as dominating the fact. Moreover, he makes his account relevant to today's problems by devoting a large part of the book to focusing "attention on the conceptual evolution of five principal issues that . . . dominate nutritional thinking until our own time". In doing so he has chosen well, and his discussions on the concept of an adequate diet, on protein and on the origins of the dietary thermogenesis controversy (recently revived in *Nature*) are all very valuable.

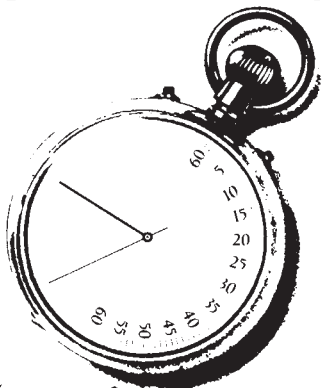
I am slightly disappointed by the fact that, inasmuch as he looks beyond internal imperatives for the growth of nutritional science, his horizon is the parallel growth of ideas in other areas of science. Highlighting this feedback is valuable, and he provides the best discussion of such interactions that is available in a popular work. But it is a pity that he did not extend his view and concentrate more on general social history and the extent to which nutritional science was also moulded by the general ethos of the society in which it was developed. In his failure to do so, his work raises questions it cannot answer. For example, his treatment of the evolution of concepts of protein and energy metabolism in the nineteenth century, while meticulous and well worth reading, is for me incomplete. I cannot believe that the subject can be fully explored without discussion of the social values that predicted it, stimulated both the research and its acceptance, and dictated its conceptual framework. Nutrition developed in the new Europe where both workhouse and standing army grew up, and the state required dietetic advice on subsistence requirements for the poor, and optimal provision for its fighting men.

It is surely no coincidence that in this environment nutritionists adopted models which involved the idea that both minimal



Skeleton of a rachitic male, depicted by A. Vesalius in *Tabulae Anatomicae Sex* (1538). Rickets was apparently so prevalent that Vesalius regarded the skeleton, of an adult with late rickets, as normal.

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(subsistence) requirements and higher optimal intakes existed? And surely the tenacity with which they clung to the idea of a special role for protein related to the social value of protein food such as meat.

But for all that Professor Guggenheim's book does not provide any solutions to such problems, it makes it clear that they exist to be solved. I hope the fluency and clear erudition of this book will encourage others to read it, to consider the same questions and, perhaps, to provide some answers. □

John Rivers is a Lecturer in the Department of Human Nutrition at the London School of Hygiene and Tropical Medicine, University of London.

Hectares for whom?

John Andrews

Farming and Wildlife. By Kenneth Mellanby. Pp.178. ISBN 0-00-219239-X. (Collins: 1981.) £9.50. *Countryside Conservation: The Protection and Management of Amenity Ecosystems.* By Bryn Green. Pp.249. ISBN hbk 0-04-719001-9; ISBN pbk 0-04-719002-7. (George Allen & Unwin: 1981.) Hbk £13, \$35; pbk £6.95, \$17.95.

SINCE prehistoric times, agriculture has been the major modifier of the world's terrestrial habitats; even the marine environment has been affected by the run-off of silt, organic nutrients and latterly of agrochemicals. In those countries where there is an active nature conservation lobby, relations with farming interests have become progressively more strained over the past 30 years as modern agricultural techniques have made rapid inroads into wildlife communities which had long co-existed with traditional farming methods. Inevitably, both sides have tended to misrepresent the situation to some degree and Professor Kenneth Mellanby's *Farming and Wildlife* provides a valuably calm and dispassionate appraisal of the effects of each on the other.

The opening chapters of the work deal in general terms with the impact of man on Britain's natural habitats and wildlife over the last 7,000 years, and more specifically with the effects of changing methods in arable farming, grassland management and livestock production since 1945. Greatly increased productivity from existing farmland has been won at the expense of a vast reduction in the population of until recently common and widespread wildlife, of which our native flowers and butterflies are perhaps the most regretted loss. At the same time, the profitability of farming and the incentives of grant aid have brought much marginal land into intensive production, severely reducing many species which were already

rare. The middle section of the book looks in some detail at the features of typical lowland farms over which most public concern has been expressed — the soil itself; hedges and trees; and ponds, rivers and marshes.

Thus far the book contains much that will come as news to farmers who are often profoundly ignorant about the wildlife on the land and their own effects on it. By contrast, the final section contains much to inform the concerned but often equally ill-informed public about pests and pesticides, diseases of livestock and about field sports, which indirectly contribute to the retention of habitats and hence of wildlife in the countryside.

Farming and Wildlife is well illustrated and readable. No doubt conservationists will read it. The question is, will farmers?

Professor Mellanby deliberately eschews the political aspects of farming and wildlife, in particular the questions of whether increased agricultural output is economically justified and whether society should be able to control rural land use change where public loss of amenity is significant. However, these questions are examined with skill and relish by Bryn Green in *Countryside Conservation*.

It is timely that conservation, which has become an increasingly complex and skilled profession, now has its first textbook, and entirely apposite, given that the conservation movement is fighting desperately for what it believes in, that the textbook should also be a confident and well-argued assertion of its case.

Part 1 is devoted to conservation concepts, the impact of man on his environment and the development of conservation in Britain. In Part 2 the author examines the characteristics of natural ecosystems and explains the impact of land use change on all our major habitat types: agriculture figures largely, but forestry, industrial and urban development, recreational impact and pollution are given comparably thorough coverage. Conservation considerations aside, one is reminded again that land use management in Britain, where every hectare counts, is in appalling disarray, with blinkered state agencies each pursuing its own special interest regardless of the general good.

The concluding section of the book examines the present methods for selection and protection of land of conservation importance, and argues that a new approach is required if we are to save the remaining areas of scientific importance and the natural beauty of the countryside.

A welcome departure from the somewhat petulant "smocks and windmills" approach of some recent writers, Bryn Green's book contains much to instruct and to inspire a hard-headed approach to the massive problems which the conservation movement now faces.

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Why should anyone care about extinctions?

Kenneth Mellanby

Extinction: The Causes and Consequences of the Disappearance of Species. By Paul and Anne Ehrlich. Pp.305. ISBN 0-394-51312-6. (Random House, New York: 1981.) \$15.95. To be published in the UK in April 1982 by Gollancz.

PROFESSOR Paul Ehrlich is a distinguished entomologist, known for his meticulous studies of butterfly populations. He is also known to a wider public as a leading prophet of doom. Fortunately, when he has been rash enough to fix dates for particular disasters, his prophecies have seldom been fulfilled. Thus in an article published in 1969 he forecast that "there had been the final gasp of the whaling industry in 1973 . . . by 1977 the annual yield of fish from the sea was down to 30 million tons . . . by September 1979, all important life in the sea was extinct [and] Japan and China were faced with almost instant starvation . . .". Now marine pollution has had harmful effects, but the oceans are probably as productive today as they were 12 years ago.

Yet sensible men must agree that our species is increasing in number too rapidly, and that the world's resources are being used too wastefully. The horrors foretold by Ehrlich and others are still possible unless populations are controlled and resources safeguarded. However, I believe

that exaggerated statements of imminent disaster are generally counter-productive. Instead of acting as warnings, they actually induce the complacency they are trying to prevent. They have contributed to what another author has recently described as "a waning of public enthusiasm in America for environmental issues".

In this latest book, Paul and Anne Ehrlich are still concerned with problems of global survival, but they restrict their attention to the way in which man is eliminating many species of plants and animals which coexist with him on the surface of the Earth. They avoid any more rash forecasts of dates when extinctions will occur, and even suggest that we may have 15 or so years to put our house — our globe — in order. They do, however, fear that the rate at which species disappear will accelerate, particularly in the tropics where vast areas of forest are being felled. Few scientists will disagree with their general forecasts of the extinction of species, though their views on the effects on life on Earth are less generally acceptable.

Extinctions have always taken place. There is little doubt that the vast majority of species which have evolved during the 3,000 million or so years during which life has existed on Earth are extinct. Some have suggested that we should therefore not worry about further extinctions; they believe that new organisms suited to

today's world will evolve to fill the vacant niches. Unfortunately this is unlikely, because man produces such sudden changes that there is no time for new forms to evolve. Thus the Ehrlichs point out that much as we may regret, from an aesthetic and scientific standpoint, the passing of the dinosaurs, their place has been taken by mammals and birds. If today we kill off the remaining elephants and rhinoceroses, the world's fauna will be depleted before any replacements have appeared.

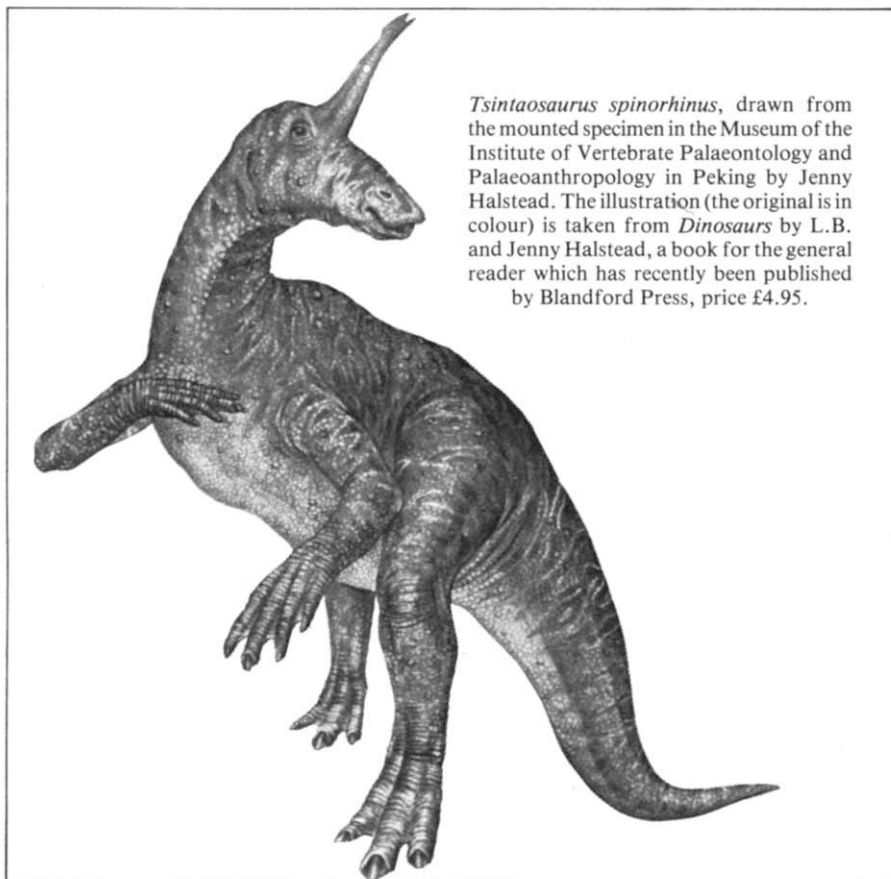
As a conservationist I regret all extinctions, whether locally as of the large blue butterfly in Britain, or globally, as of the dodo, the great auk or the passenger pigeon. I wish I could help to reverse the trend. But we must accept that the majority of people do not care, and in fact are doing much to accelerate the process. How can we convince them of the error of their ways?

The Ehrlichs give four reasons. First, compassion — all species on "Spaceship Earth" have an equal right to exist. Second, aesthetic and spiritual — wildlife contributes to the beauty and interest of the world. Third, economic — many organisms, their potential as yet unrecognized, may be exploited as food or other resources, or may provide essential genetic material for crops, livestock or drugs. Fourth, and in the Ehrlichs' view most importantly, by eliminating other species man is endangering the whole global life-support system, and so rendering our planet increasingly inhospitable to man himself.

What do we mean when we say that all species have an equal right to exist? Logically this would mean that man must do nothing to decrease their numbers or to reduce the area they inhabit. Even those who, for religious reasons, do not kill, farm the land; this can cause local or even general exterminations. If it is the species which has rights, then I suspect that we like to retain some members more for our purposes than for their own.

The Ehrlichs' second reason really boils down to saying that we wish to preserve the species which give us pleasure. This pleasure may have its spiritual or even its religious components, but it acknowledges that we conserve wildlife for man's satisfaction and not for the benefit of the wild creatures themselves.

The statement about the possible economic value of wildlife has some substance. Deer and antelope are proving more efficient converters of some types of vegetation than are cattle or sheep; there may be other animals which will be profitably domesticated. Man has been very conservative in his choice of food crops, and other wild plants may be valuable sources of food. Genes of wild plants may confer valuable properties to existing crop species, so wild grasses and Andean potatoes should be preserved. Unfortunately the species of wildlife for whose preservation most effort is being



Tsintaosaurus spinorhinus, drawn from the mounted specimen in the Museum of the Institute of Vertebrate Palaeontology and Palaeoanthropology in Peking by Jenny Halstead. The illustration (the original is in colour) is taken from *Dinosaurs* by L.B. and Jenny Halstead, a book for the general reader which has recently been published by Blandford Press, price £4.95.

made — the large carnivores and herbivores — would seem to have less potential except to provide pleasure and inspiration. But it is obviously good sense to try to preserve large areas of tropical forest and other habitats which contain thousands — perhaps millions — of undescribed species, whose economic potential has not been studied.

Finally, the Ehrlichs believe that unless we can maintain the diversity of the world's flora and fauna, the whole life-support system may break down. This is probably true, but the organisms which are the most important — the decomposers in the soil, insignificant parasitic insects, soil fungi and sewage organisms — are seldom the subjects of popular conservation programmes. The impoverishment of our fauna with the loss of the wolf, the bear and

the wild boar has *not* had the effect of making farming in Britain less efficient — quite the reverse.

So we must come to the conclusion that conservation is a far from simple subject. The economic and similar arguments often need to be qualified. Those based on the value of diversity are far from proven. Conservationists must avoid making statements which they know to be untrue in an attempt to obtain wider support from politicians and the general public. The most cogent reason for conservation, in my opinion, is that "man does not live by bread alone"; the general and aesthetic reasons have more validity than the economic. □

Kenneth Mellanby's most recent book is Farming and Wildlife (Collins, 1981).

Fighting for the conservation of tigers

Brian Bertram

Saving the Tiger. By Guy Mountfort. Pp.123. ISBN US 0-670-61999-X; ISBN UK 0-7181-1991-6. (Viking/Michael Joseph: 1981.) \$16.95, £7.95.

THE tiger is a slim, dramatic animal, and it now has a book to match it. The numerous, large and well-printed colour plates are spectacular and superb. They do not leave a great deal of space for the authoritative text, in which the author summarizes our still scanty information on tigers, their appalling conservation plight and international attempts to prevent their extinction.

Despite the title, the tiger has not been saved, and it would be dangerous to think that it had been. Equally, it would now be much closer to extinction but for international efforts on its behalf. Guy Mountfort was both the catalyst and the power house in setting up Operation Tiger in 1972, under which the World Wildlife Fund raised nearly a million pounds for tiger conservation. He describes how the governments of India, Bangladesh and Nepal were persuaded to establish reserves for tigers, and other countries of South-east Asia have since followed suit.

The hunting of tigers for sport is no longer a threat, thanks to national legislation in most of the countries concerned. The traffic in tiger skins for the fur trade has dwindled, thanks also to CITES, the Convention on International Trade in Endangered Species. Illegal killing of tigers is declining as local policing improves and as there is less direct contact between tigers and the local populace. The main threat nowadays is from loss of the forest habitat and the prey species on which tigers depend. Through the efforts of Guy Mountfort and others, this threat has been alleviated in many areas, and general

public awareness of the plight of these wonderful animals has been raised.

What about future prospects? First, our priorities. With great difficulty and organization, large sums of money have been raised and thousands of square miles of tiger habitat protected. The total costs involved are equivalent to those needed to build a mere half-dozen miles of motorway. Which is more important? Should we have some form of conservation levy which because we human beings are so numerous would be paltry at the individual level?

Second, the status of tigers in their native reserves is relatively safe only so long as there is no breakdown of law and order in the countries concerned, and until human population pressures become irresistibly strong.

Third, although the many captive tigers in the zoos of the world are not a substitute for wild populations, they may well be a back-up. There should be tigers in the wild where they belong. But if the 350–400 wild Siberian tigers or the 600–800 wild Sumatran tigers are exterminated through human greed or folly, there are at least 800 Siberian and 150 Sumatran tigers in captivity. I am convinced that these could be used to re-stock areas from which wild tigers had been wiped out. Certainly, it would be difficult, and would need money, time and skill, and certainly there would be failures. But there is no reason in principle why, if necessary, reintroduction should not prove possible with tigers as it has with other large cats. We only hope that it does not become necessary. Guy Mountfort has done much more than most to help prevent it. □

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The sexes look at sex

Adrienne L. Zihlman

The Woman That Never Evolved. By Sarah Blaffer Hrdy. Pp.242. ISBN 0-674-95540-4. (Harvard University Press: 1981.) \$17.50, £12.25. *The Evolution of Love.* By Sydney L.W. Mellen. Pp.312. ISBN hbk 0-7167-1271-7; ISBN pbk 0-7167-1272-5. (W.H. Freeman: 1981.) Hbk \$15.95, £8.50; pbk \$8.95.

BOOKS on the evolution of human behaviour are often more interesting for the questions raised than for the answers proposed. This is particularly true when one compares the questions posed by male and female authors about the evolution of primate sexuality. The books under review provide a classic case study in contrasting, almost mutually exclusive, viewpoints.

During the 1960s, male reconstructions of human evolution informed us that human hairlessness evolved to enhance front-to-front sex; that men's social and political clubs have sprung from the co-operative camaraderie of the male hunting groups that made our species successful millions of years ago; and that human females lost oestrus and became perpetually sexually receptive so as to keep males around to provide protection and meat from the hunt.

During the 1970s, women increasingly joined men in the game of replaying human prehistory. In place of the prevalent Man-the-Hunter scenario that put males centre stage and relegated passive, dependent females to the wings, waiting for the heroes' return, women anthropologists emphasized the important social and economic role of Woman-the-Gatherer. They also drew on sociobiological theory, which hypothesizes that the sex investing the most time and energy in raising the offspring makes the choice of mates. The central male role in the evolution of human culture and institutions was disputed by field observations on primates and on gatherer-hunters such as the !Kung San, revealing the pre-eminent involvement of females in obtaining and sharing food, choosing mates, socializing children, establishing and maintaining social networks, and using tools — in contrast with the earlier image of females as rather passive recipients of male sexual and hunting activities.

Sydney Mellen's *The Evolution of Love* and Sarah Hrdy's *The Woman That Never Evolved* provide examples of the male and female viewpoints of the 1980s. Both are concerned with an evolutionary overview of human nature, particularly sexual nature. Both use the theoretical framework of sociobiology, which attempts to explain contemporary human behaviour by genes that evolved millions of years ago. Mellen draws heavily on the fossil and archaeological record of the past 2–3 million years and does not dwell on non-human

primates, whereas Hrdy goes deeply into the observed behaviour of females of numerous primate species and makes little reference to evolution as read from the fossil record.

According to Mellen, "love" emerged some three million years ago as an important adhesive force for human social groups and for successful child-rearing. His definition of love slides between conscious emotional attachment and sexual attraction; the large human brain is implicitly involved, but how human love differs from the emotional bonds of higher non-human primates is not always clear. His shortest chapter (7 pages) is titled "Love Between Parents and Children", the longest (46 pages), "The Enigma of Homosexual Love", by which he means male homosexual love.

Mellen's book belongs with the 1960s genre in that the framework is Man-the-Hunter and male choice of females. A central issue is male access to females, in order to be assured of their procreative potential, sexual receptiveness and "love". Hunting is credited with our acquisition of intelligence, cooperation, communication and food-sharing (old stuff); and (a new twist) men had many mates and natural selection enhanced "capacities for suspending fear" which resulted in the surviving hunters passing on "their courageous genes . . . to many sons". Sociobiological theory tends to find a gene for every behaviour, and so Mellen explains that "finally the world came to be rather full of men whose chromosomes carried certain invidious genes for preferring young women", surely an unnecessary exegesis in a world in which, until very recently, few females or males lived beyond the age of 30 or 40.

The Woman That Never Evolved challenges some of the sexual stereotypes that Mellen perpetuates, almost to the point of reversing them. Hrdy argues that the ubiquitous domination of females by males is a product of primate evolutionary history, as male domination is the rule (with few exceptions) among non-human primates. She brings together a broad array of up-to-date information on females of many species, from galagos to gelada baboons. Of particular interest are the chapters on monogamous primates, among which females enjoy relatively privileged positions, and on those species such as lemurs and squirrel monkeys in which there is no clear dominance of males over females.

Hrdy lays the greatest emphasis on female competition and status-seeking, as though to prove that women have inherited all the same undesirable traits that men possess and therefore should be equally successful. She states that "competition among females is central to primate social organization", and that "every female is essentially a competitive strategizing creature". Obviously, all members of a group "compete" to some extent for food,

status and sexual partners, but, as in an atomic nucleus, the disruptive forces must be less than the cohesive ones if the group is to survive. In most species, male access to females is more limited than female access to males, hence male-male competition would be expected to be, and is observed to be, more intense than competition among females.

Hrdy's evolutionary construct is reminiscent of those of the 1960s, with a sort of reversal of roles. It is females rather than males who are competitive and status-seeking, but instead of forming clubs and political parties, they use their sexuality to gain power and domesticate males and keep them from killing their infants. Hrdy's observation that "outside" male langurs will sometimes take over a troop and kill the offspring of lactating mothers — presumably so that they can re-impregnate these females with their own genes — is raised to the level of a paradigm: by the iron laws of sociobiology, primate males will try to "murder" offspring not their own and must be prevented from doing so by female strategems.

The woman that never evolved, according to Hrdy, is the woman invented by contemporary feminists: "created equal", having a natural sense of solidarity with other women and innocent of the male lust for power and status. Hrdy seems to assume that culture plays no role in the behaviour of women, and if certain kinds of behaviour are not found in other primates, they will not be found in humans.

I have improvised a dialogue between Mellen and Hrdy, to contrast their

concerns and conclusions. Mellen: "Protohuman females were evolving in the direction of ever-increasing care and nurture of the young". Hrdy: "The vision of assertive, dominance-oriented females differs radically from existing stereotypes of female primates as non-stop mothers whose perennial preoccupation with nurturing offspring keeps them out of politics". Mellen doubts that pleasure from sexual intercourse is common for women. Hrdy retorts that female sexual activity is "assertive and temporarily insatiable".

Both of these books join the growing stacks of sociobiological attempts to integrate genes and human behaviour. They fail by ignoring the intervening levels that influence the outcome of behaviour — development, socialization, symbols, ritual and values that are passed on non-genetically from generation to generation. Instead, they invoke hypothetical genes evolved either by hypothetical Pleistocene screenplays or deduced from selected observations on non-human primates and contemporary cultures. Mellen and Hrdy draw nearly opposite conclusions from their gene-based reconstructions. The book that has not yet been written is one that recognizes several levels of analysis, that integrates culture and biology and that interprets female and male behaviour in a mutually adaptive social system. □

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Taste for travel and a naturalist's eye

A.J. Cain

The Roving Naturalist: Travel Letters of Theodosius Dobzhansky. Edited by Bentley Glass. Pp.327. ISBN 0-87169-139-6. (American Philosophical Society, Philadelphia: 1980.) \$8.

THEODOSIUS Dobzhansky was a truly remarkable man, of great personal experience, shrewdness, humanity and intellectual ability. He wrote clear, vigorous, masculine prose, expressing the forceful thoughts of a first-class observer. This book of his letters and reminiscences is a delight; one can dip into it anywhere and find oneself in grand company. Even when his reactions are the usual ones — to the grandeur of tropical forests, the horrors of temperate-zone poverty or "lousy bureaucracy" — he expresses them with a freshness that always precludes banality. The book would be excellent at one's bedside for those with strength enough to ration themselves to a single letter.

There is an excellent, short biographical

introduction by Bentley Glass which gives the major events in Dobzhansky's extraordinarily varied and interesting life-history. He was born in the Ukraine in 1900. In 1910 the family moved to Kiev. The boy, already a keen butterfly collector, went on a school excursion to the Caucasus; two years later he and a friend went off by themselves without parental permission to that fascinating region. His tastes for travel and entomology were already developed.

As a student at Kiev University, supporting his widowed mother, he had a difficult time towards the end of the Great War, and during the Revolution, in 1919, they experienced the Communist terror. Typhus, the invasion of the Polish Army, the death of his mother and severe privations in the winter of 1919–1920 were serious afflictions which he survived, becoming a private tutor, a graduate, an assistant to one of the professors of zoology and a tutor in the Workers'

Faculty. Soon after, he visited Moscow to see the genetical researches of Chetverikov and his group, who had stocks of *Drosophila* given to them by H.J. Muller. Then he migrated to Leningrad, and was sent on scientific expeditions to Central Asia to study genetic variation in domestic animals — he seems to have studied nearly every other biological phenomenon as well, especially human beings. The first part of this book is his enthralling reminiscences of his travels in Central Asia between 1925 and 1927. In 1927 he and his wife went to the USA to work with Thomas Hunt Morgan at Columbia University, and he began that illustrious career in population genetics using *Drosophila*.

The problems arising from his investigations into populations of *Drosophila* in the USA demanded wider genetical explorations. The letters in the book (unfortunately we are never told to whom they were written, which would often clarify their mode of treatment of some topics) were written on his visits to Brazil (1948–1953), to other countries of South America (1955–1958), to Israel, Lebanon and Egypt (1956) and India, Indonesia and New Guinea (1960). He must have been a superb correspondent. As is to be expected, since the reminiscences were taped later in his life and the first letter dates from 1948, his character, after the sometimes hair-raising experiences of his youth, was fully formed. Thus we see no development of character in the book any more than there is in, for example, the short stories of "Saki", but the absence of that is more than compensated for by being able to see through the eyes of so good an observer and writer such a variety of landscapes, organisms, people and situations, sometimes hilarious, often exasperating, but always exciting.

He had a naturalist's eye for animals, plants and people, and excellent appreciation of landscape (less so for geology), a sharpness for human (as well as animal) character, and a lovely dry humour, very like "Saki's", all of which come out just as well in his letters as they did in his conversation. No empty pomposity ever imposed on him, and not many other involuntary psychological deceptions. The freshness of his response to tropical nature seems at first naive (but never boring, gushing or silly) because it is so immediate, but naive he was not. He turned a sharp eye inwards on himself as well — there are some extremely interesting *obiter dicta* on his own reactions to mountains, uninhabited tropical islands, palms, the tropical night and the Holy Land.

Dedicated drosophilists must be warned that there is little in the book about *Drosophila*. Everyone else will find a lot in it. □

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Missing the essential Professor Eysenck

P.E. Bryant

Hans Eysenck: The Man and His Work. By H.B. Gibson. Pp.275. ISBN 0-7206-0566-0. (Peter Owen, London/Humanities Press, New Jersey: 1981.) £11.95, \$26.

THE mainspring of the considerable body of research carried out by Professor Eysenck and his colleagues has always been his theory of personality. This is based on two ideas: the first is that everyone's personality can be described in terms of the person's position along three separate dimensions, and the second that the mechanisms which underlie these dimensions are, in principle, discoverable.

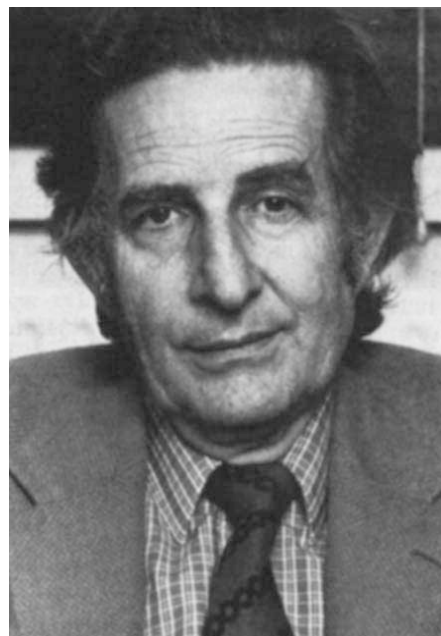
None of the specific details of his account of personality — the use of factor analysis, the three dimensions of introversion–extraversion, neuroticism and psychoticism or the use of the notions of excitation and inhibition and, later, of arousal to explain these dimensions — was in itself particularly new, but it has led to a great deal of original and fruitful research and it has also propelled Eysenck into a series of major controversies.

Anyone who has spent half-an-hour or more with one of his many books will know something of the theory and will also have learned that Eysenck not only revels in these controversies but also writes about them vividly and lucidly. Such characteristics are a distinct advantage in a psychologist. Controversy is the life-blood of psychology. The subject is still finding its feet, and this means that nothing much is certain and nothing can be taken for granted. Every single claim has to be argued over.

No one has recognized this or demonstrated it more than Eysenck. He is nettled, and often quite rightly, by anything that looks like a respectable consensus. It has been the established academic view that individual differences are rather unimportant in psychology, that people with extreme left-wing views are very different in personality from people on the extreme right, that psychoanalysis works, that a person's intellectual abilities are largely determined by the environment in which he grew up, that astrology is bunk and that smoking is a cause of cancer. Eysenck has at various times disagreed quite violently with all these respectable sentiments, and whether or not his objections are right they are always argued cogently.

His relish for battle and the clarity with which he presents his blow by blow accounts of them to psychologists and laymen alike represent an important contribution to psychology, but there is much more besides. He, more than anyone, shaped the development of clinical psychology in this country. He, too, fought valiantly and successfully against the unfortunate tendency among psychologists to

break up into quite separate camps which do not talk to each other and which pursue different questions with quite different methods. Eysenck insisted that the question of personality was too important to be left just to the personality testers. The methods of experimental psychology, he argued, were also needed to explain why people are different from each other. He managed to build a bridge between the two camps which has lasted extraordinarily well, so that nowadays no one using personality questionnaires can afford to



Camera Press

Hans Eysenck — "nettled . . . by anything that looks like a respectable consensus".

ignore laboratory research just as no one doing laboratory experiments can resort to the easy assumption that what is true about the behaviour of one person is true as well of everybody else. This link between two hitherto separate disciplines is in my view Eysenck's greatest achievement.

Such a man obviously deserves the accolade of a biography, and H.B. Gibson's account of Eysenck's life coming out as it does near to his retirement ought to give us a good idea not only of Eysenck's own development but also of his considerable influence on psychology over the last three decades. But it does not. Gibson's book is at its strongest when it recounts the simple facts about Eysenck's life — his early upbringing in the Weimar Republic and then under the Nazi regime, his revulsion against the Fascist system and his consequent move to England, his decision *faute de mieux* to study psychology (*mieux* in this case being physics), his early work with Burt and then his subsequent move under the tutelage of Aubrey Lewis to the Institute of Psychiatry in order to set up the clinical psychology department there.

But we need to know more than that and

in particular we ought to be told in some detail about the controversies that have taken up so much of Eysenck's academic life, and also about the kind of man he is. On both these counts Gibson's book is a clear failure. He hardly deals with the controversies at all. Eysenck's own views are described reasonably well but the arguments about them, though sometimes mentioned, are never pursued, and again and again Gibson resorts to the excuse that the issues are too complex for his book. This is indeed an unfortunate contrast with the subject of his book who has never hesitated to introduce the layman to exactly the issues which Gibson so consistently avoids.

Thus one of the most obvious opportunities of a book like this — the chance to see how psychology has advanced with the help of lively debates seen through the life of one of its main controversialists — is almost totally lost. Worse still, at times the book's account of Eysenck's controversies is quite seriously misleading. For example, there is a chapter called the "Psychology of Politics" which deals with two very disparate topics. One is Eysenck's theory, published in the 1950s, of the personality types associated with various political views, and in particular his amusing claim that right- and left-wing extremists have much in common, a suggestion which did not endear him either to the left or to the right. The second is the debate about the question of the relative effects of heredity and environment which Eysenck formed so vigorously in the 1970s. As far as I can see, Gibson's only reason for putting these two issues together is his idea that one of the reasons for the violent hostility which greeted Eysenck's views about the importance of heredity was the vindictive rage felt by left-wing elements at the earlier suggestion that they were brothers under the skin of the Fascist foes. There may have been people as lunatic as this, but there were also some serious, well-argued objections which we are not given. We hear about the riots and the punches, but not about the debate.

Nor is the book much more helpful about Eysenck's own personality. It seems that over the years he fell out with many of his important colleagues, but the reasons why remain obscure. Eysenck is apparently shy: yet he has the habit of making outrageously immodest, public claims about his own abilities. Gibson has no explanation for this seeming paradox. Another issue which is left quite unsettled concerns Eysenck's attitude to other people. Gibson takes pains to show how kind Eysenck can be, and often the book adopts the style of a life of one of the saints as it ramblingly recounts this or that good deed by the professor. St Francis gave his cloak to a poor man: Eysenck took a whole day off to fetch a colleague's baby from hospital. But the book also relays some ungenerous comments made by Eysenck about and sometimes directly to other people. I simply do not know what to conclude, and

yet the question is important because one of the major reasons for Eysenck's success has been his ability to keep a large number of people around him working with enthusiasm on his ideas. I should have liked to have known how he did it.

Gibson's book is interesting and often

entertaining. But it gives us nothing like a proper assessment of Eysenck's formidable contribution to psychology over the past three decades. □

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Archaeology in retrospect and in prospect

J. Desmond Clark

A Short History of Archaeology. By Glyn Daniel. Pp.232. ISBN 0-500-05041-4. (Thames and Hudson: 1981.) £9.50, \$17.95. *Antiquity and Man: Essays in Honour of Glyn Daniel.* Edited by John D. Evans, Barry Cunliffe and Colin Renfrew. Pp.256. ISBN 0-500-05040-6. (Thames and Hudson: 1981.) £25.

It is probably true to say that no school of archaeology has done more in the decades immediately preceding and following the Second World War than has that at the University of Cambridge. There are the unique contributions of Grahame Clark to understanding Mesolithic and Neolithic economy; of Charles McBurney to Palaeolithic studies through his excavations in North Africa, Iran, Afghanistan and Britain; of David Clarke in revolutionizing theory and concepts in archaeology; and of Glyn Daniel through his special interest in and encyclopaedic knowledge of the history of archaeology and the study of megalithic monuments.

These were scholars unsurpassed in their fields and their experience, knowledge and teaching have been responsible for the training of an unrivalled nucleus of the leading archaeologists working in the Western world today. In part this stems from the alliance between archaeology and anthropology that has always been present at Cambridge and the success of archaeological interpretation and model building has come from the understanding of human behaviour provided by ethnographic studies, not infrequently now being undertaken by the archaeologists themselves. While archaeology derives much of its methodology from the natural and earth sciences, interpretation can only come from the insights of the anthropologist. When Professor Glyn Daniel retired this July after 8 years in the Disney Chair at Cambridge and 35 years on the faculty, an era in British archaeology drew to a close. A new group of scholars, often his own students, have taken up the challenge of the modern, conceptual approach to the discipline and are among the leading contributors to it.

There is no one who has made more of an impact than Professor Daniel on our understanding of the history of archaeology and the way that this has influenced current theory, and on the story of its emer-

gence from the enveloping strait-jacket of the Book of Genesis to become the creative and exciting discipline it is today. To celebrate his general editorship and the appearance of the hundredth volume in the *Ancient Peoples and Places* series published by Thames and Hudson, he has produced *A Short History of Archaeology*.

The volume is divided into five main chapters that cover the growth of archaeological method and theory from the beginnings, through the formative and then the developmental years between the wars, to that of the "new and not-so-new archaeology". This is a well-written, witty and enjoyable summary of the main conceptual, analytical and methodological advances in the field of prehistoric and historic archaeology as manifested by accounts of the increasing numbers of significant and often very exciting finds, the development of survey, excavation and recording techniques, and the awakening interest of the general public. In other words, it is an excellent history of mankind's ideas about his ancient past. This approach enables archaeologists to appreciate the value of the historical framework that has made possible the advances in field work, analysis and interpretation of the past two decades. By trying to understand the tenor of intellectual thought at a particular time we are better able to appreciate the major developments in archaeological theory and the reasoning that lies behind them.

Following the ordering of assemblages of artefacts in the Three Ages System, to that of the Stage or Age based on stratigraphic excavation and the concept of the "type fossil", archaeology has moved on to determining patterns of economic and social behaviour. The major concern with chronology and time-depth, which for so long occupied the earlier archaeologists, has only been removed since the availability of techniques such as radiocarbon, potassium-argon and the palaeomagnetic reversal chronology made possible by physicists, chemists and geologists since 1950. We are now, therefore, in a position to know, even if we cannot comprehend, the magnitude of the time involved in the story of our biological and cultural evolution.

A Short History of Archaeology is a synthesis not only of the record for

Western Europe but sets out to cover most of the world where archaeologists have made significant contributions. Thus the history of archaeology in the Americas, Africa, the Middle and Far East, and Australasia is discussed, though more satisfactorily for some areas than for others, depending on the author's viewpoint. The dramatic discoveries of Layard, Schliemann, Petrie, Howard Carter, Arthur Evans and a host of others help to show the way in which archaeology has advanced from an over-emphasis on artefact morphology and typologies to the attempt to learn about the behaviour and the individuals that lie behind the tools themselves. The contributions of the systematic excavators and recorders — Pitt Rivers, Petrie, Mortimer Wheeler — and of those who sought to understand the processes behind culture change like Gordon Childe and the ethnographers receive here the credit they deserve.

Only in the last section of the book on the "new archaeology" does one get the impression that the author is not really in sympathy with his subject. Even though there is not all that much which is new in the more theoretical frameworks and the problem-orientated archaeology of today, it is the emphasis on this problem-orientated approach, coupled with the great advances in technique and method such as "edge polish" studies, spatial analysis, taphonomy and experimental archaeology, that is bringing about such an important re-orientation in our attitudes.

One thing that stands out from Glyn Daniel's intensive search of the literature is the way in which the intellectual world becomes receptive to new hypotheses and new constructs only when it is ready to do so and, although others before may have made the same observations and drawn the same conclusions, unless the scientific world is waiting for them they are quickly forgotten. The manner in which preconceptions can retard true understanding of the evidence is well seen in the early interpretation of Neanderthal man and the ease with which the Piltdown hoax was perpetrated. Glyn Daniel has led the way in showing that archaeology can be of interest for the layman as for the specialist and his works have been the forerunners of those *hautes vulgarisations* — accounts of all those prehistoric discoveries and palaeoanthropological wranglings — that delight the public today.

An excellent, well-selected set of colour and black and white illustrations accompany the text and this will certainly be a standard introductory textbook for years to come.

Antiquity and Man is not the usual kind of *Festschrift* which, all too often — as Glyn Daniel himself has said — is "a cemetery of articles which ought to have been published elsewhere in more accessible form, or not at all". The Prince of Wales, who took the archaeology Tripos Part I at Cambridge and was taught by

Glyn Daniel, contributes a foreword, and essays by some 28 leading authorities on archaeological topics and other matters make up the volume. The subjects treated are of direct interest to Glyn Daniel who has had a major involvement with and made a great impact on most of them. It is both a stock-taking of the state of archaeology in the continents today and a discussion of some of the leading theories that lie behind recent advances.



Glyn Daniel, who retired earlier this year after 35 years at Cambridge.

The book is divided into four unequal parts and comprises a valuable series of summary papers on a range of topics which show the extent of Professor Daniel's interest in and contributions to the discipline and also to Cambridge with its college dons and undergraduates. Space does not permit — and it would be invidious to single out — individual contributions from this outstanding text, but the first part contains several excellent summaries of the current state of archaeology in Europe and the Middle East, Africa, Australia and China. The reader is made to appreciate the contribution of the Cambridge School to the changing face of archaeology today in Third World countries — the need for the training of nationals to take over from the expatriates and the advantage for both of collaboration and the multidisciplinary, international team approach. Several authors make a plea for fieldwork and warn against its neglect in favour of the theoretical approach which is sometimes only too evident today. Fieldwork is indeed the life blood of archaeology, and models and hypotheses are worthless without the factual empirical data that come from meticulous field methods and objective analysis and interpretation.

Part II comprises nine essays on current theories concerning the construction of megaliths found from the central Mediterranean to Britain and Scandinavia. Glyn Daniel played no small part in elucidating the mystery of their origins and significance. This section will be of especial interest to European archaeologists and

shows well the shift in emphasis from the monuments themselves to attempting to learn about the populations that built them and the different economic and social organizations that gave rise to these ritual centres, often associated with communal burial. The diffusionist theory for the spread of megaliths has now been largely replaced by one of local, autochthonous development, while the radiocarbon and TL ages now available show that, far from being derived from the eastern Mediterranean, the megalithic complex preceded in its inception the major monuments of the Ancient Near East.

Part III sets out Glyn Daniel's influence in many different ways in awakening and stimulating public interest in archaeology: as an editor, particularly of the *Ancient Peoples and Places* series, as an "anchor man" of the television programme *Animal, Vegetable, Mineral* with Sir Mortimer Wheeler and later of the *Buried Treasure* series with Paul Johnston. His influence could not have been greater than through his editorship of *Antiquity*, so ably helped by his wife Ruth as production manager. This is and will remain, it is hoped, one of the leading archaeological journals.

These essays also bring out, especially in Part IV, what is perhaps Professor Daniel's most significant contribution, namely his great success as a teacher. Many of the essays are written by his former students and the high praise and affection with which they all speak of him bears ample witness to the wit and erudition with which he enlivened his lectures and to his natural ability to produce enthusiastic and professional archaeologists who have remained his friends.

Besides being a valuable supplement to *A Short History of Archaeology*, this volume is full of entertaining asides about archaeology and publishing, amateurs in archaeology and the public image of the archaeologist. It also contains interesting information about Glyn himself, his many achievements and his progress through the *menus gastronomiques* of Brittany and the wine country of the Dordogne in his pursuit of archaeology.

Both books show very clearly how the discipline of archaeology is a product of Western European civilization. But the focus has now shifted to the Third World and other countries since it is here that we are learning what it was that made us human. It is here also that archaeology has a greater role to play than in the Western world since, for many nations, it is the most important source of knowledge of their past. Even though this may be regarded as only small beer and lentils, the record is as good as or surpasses that which has gone before. □

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ARTICLES

Superluminal quasar 3C179 with double radio lobes

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VLBI observations of the quasar 3C179 reveal that its two milli arc second components have an apparent relative velocity of 7.6 times the velocity of light. This is the fifth radio source in which 'superluminal' motion has been reported but the first which also exhibits double lobe structure on the arc second scale. Statistical arguments which apply to such sources cause difficulties for explanations based on motion in a relativistic jet.

SUPERLUMINAL motion (apparent relative velocity, $v > 2c$) has been reported for components in the milli arc second radio structure of the strong radio sources 3C345, 3C273, 3C279 and 3C120. The phenomenon has been widely discussed and reviewed¹⁻⁷ and some competing, ingenious models have been proposed to explain the illusion^{8,9}. I report here a fifth example of the phenomenon. VLBI (very long baseline interferometer) observations of the 18 mag quasar 3C179 reveal an expansion rate between its two milli arc second components of 7.6c over the course of 1.2 yr. The source has a higher redshift ($z = 0.843$, see ref. 10) than the other four superluminal sources and the core is a factor of 10–20 weaker. Unlike the other superluminal sources it has classical double-lobe morphology on an arc second scale. This work was motivated by the suggestion by Scheuer and Readhead¹¹ (repeated by Hine and Scheuer¹²) that such sources should not exhibit superluminal motions.

3C179 (=0723+67) was selected from the quasars mapped by Owen, Porcas and Neff¹³ using the NRAO Green Bank interferometer at 2.7 and 8.1 GHz. Thirty of these sources form a set with flux densities at 966 MHz ≥ 0.7 Jy, magnitudes brighter than 19 and angular sizes > 10 arc s. Nearly all these quasars have detectable, compact central components. Amongst these, 3C179 has the strongest central component of ~ 0.5 Jy, contributing $\sim 30\%$ of the flux density at 2.7 GHz, and an outer double-lobed structure with a separation of 14 arc s in position angle (PA) $\sim 80^\circ$. At frequencies below ~ 2 GHz the radio spectrum has a spectral index, α , of -0.75 ($S(\nu) \propto \nu^{-\alpha}$) but at higher frequencies the spectrum flattens, indicating the presence of the compact component. The radio spectrum, derived from a compilation of published flux density measurements and recent observations, is shown in Fig. 1. The source was not known to be variable in flux density at the time of selection but comparisons of recent measurements at 5 and 10.6 GHz with measurements made in the late 1960s^{14,15} suggest that the core is variable, both on a 10-yr and a 1-yr time scale.

Observations

VLBI observations were made of 3C179 at two epochs, 1–2 October 1979 and 9 December 1980, at a frequency of 10.7 GHz. The telescopes at Effelsberg (FRG), Haystack (Massachusetts, USA), Green Bank (West Virginia, USA) and Owens Valley (California, USA) were used, and the hydrogen maser frequency standards used at all the sites permitted coherent integration times of 4 min. The Mark 2 VLBI recording system used for these observations achieved an r.m.s. error per point of 12–20 mJy on the high resolution transatlantic baselines. The interferometer lobe spacing on the longest baseline is ~ 0.5 m arc s. In both observing sessions at least 11 h of good data were obtained at all the telescopes. The data were processed using the Max-Planck-Institute VLBI processor in Bonn and the visibility functions were calibrated using

measurements of the individual antenna gains and system temperatures.

Results

The most interesting structure in 3C179 is revealed by the high resolution transatlantic baselines. In Fig. 2a, c, e, the visibility functions measured on these baselines in October 1979 are plotted. These clearly show the oscillatory nature characteristic of a double morphology. Simple gaussian modelling of the sky brightness distribution gives an excellent fit to the visibilities with two components, of flux ratio $\sim 2:1$, separated by 1.07 m arc s in PA 92° . This orientation is within $\sim 12^\circ$ of the PA of the outer structure although the latter is not well defined as both outer components are heavily resolved¹³. This may be compared with the good alignment of inner to outer structure generally observed in the central components of double-lobed sources such as Cygnus A, 3C111, 3C390.3, NGC6251 and 3C236 (refs 16–19). However, this is the first time that the structure of the central component of a double source identified with a quasar has been determined. Those quasars which have been observed to date have asymmetric outer structure and generally show marked bending between the angles of the inner and outer structure (for example, 3C380, 3C147 and the superluminal sources 3C345, 3C273 (ref. 19)).

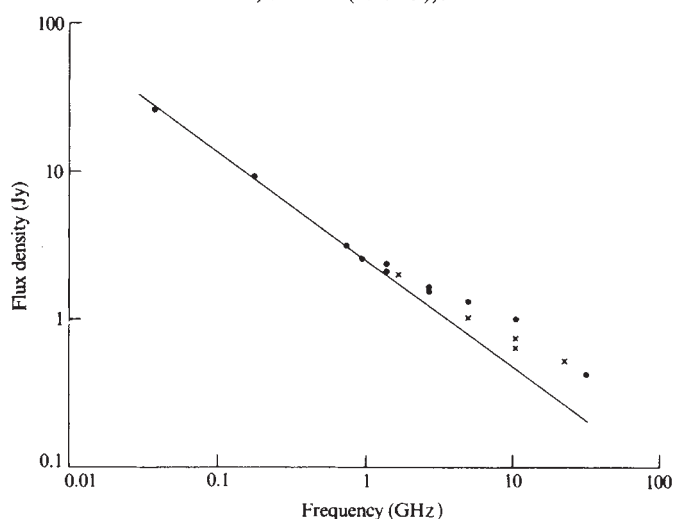


Fig. 1 The radio spectrum of 3C179. Reference numbers for measured flux densities at different frequencies are shown in parentheses. UE, unpublished measurements made with Effelsberg 100-m telescope between 1979 and 1981, marked with crosses. 38 MHz (35); 178 MHz (36); 750 MHz (37); 966 MHz (10); 1.4 GHz (37, 38); 1.7 GHz (UE); 2.7 GHz (13, 39); 5.0 GHz (14, UE); 10.7 GHz (15, UE); 22.7 GHz (UE); 31.4 GHz (40). The straight line through the low frequency points represents a spectral index of -0.75 .

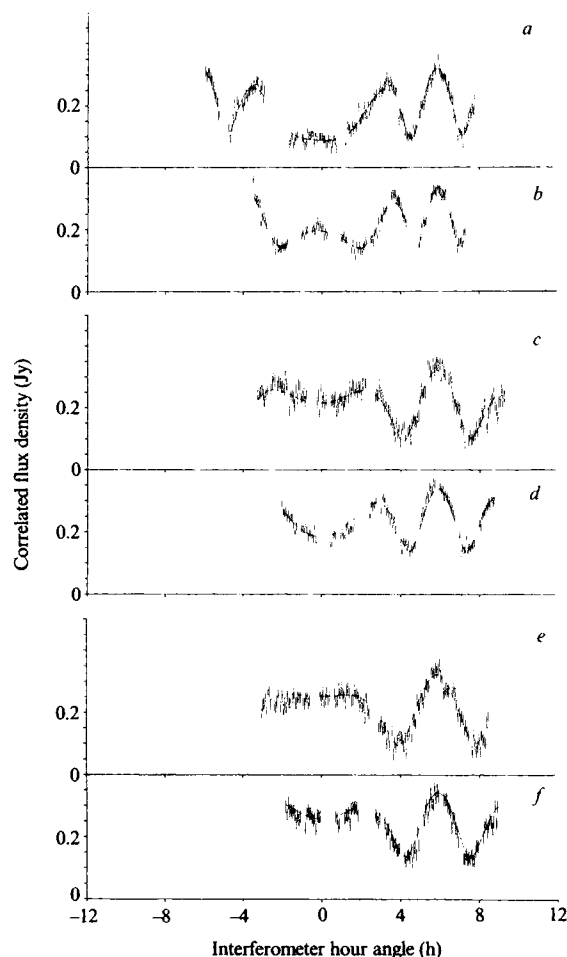


Fig. 2 Correlated flux density of 3C179 on various baselines versus interferometer hour angle. The solid line represents the best two-component fit. Baselines: *a, b*, Effelsberg–Owens Valley; *c, d*, Effelsberg–Green Bank; *e, f*, Effelsberg–Haystack. *a, c, e* were measured in October 1979; *b, d, f* were measured in December 1980.

The visibility functions for the same baselines observed in December 1980 are shown in Fig. 2*b, d, f*. Again the structure is clearly double, although it is equally apparent that structural changes have occurred. The most interesting feature is the narrowing of the distance between the peaks and troughs of the visibility function, corresponding to a larger separation of the two components at the later epoch. Gaussian model fitting confirms this, giving a separation of 1.24 m arcs in the same position angle. The results of the gaussian parameter fits to the data from both epochs are given in Table 1, along with the single dish flux densities for the whole source measured in Effelsberg. With the standard values of the cosmological parameters used in previous studies of superluminal sources ($H_0 = 55 \text{ km s}^{-1} \text{ Mpc}^{-1}$, $q_0 = 0.05$) 3C179 has an apparent separation velocity between components of $7.6c \pm 1c$. This makes it the fifth known source exhibiting superluminal motion between milli arc second components. Projecting back the separation rate gives the epoch of zero separation as ~ 1972.0 ; unfortunately, no flux

density monitoring of 3C179, which would indicate any outbursts, seems to be available for this time.

An additional change that has occurred during the 1.2 yr between the two observing epochs is the depth of the minima in the visibility functions, which have become shallower with time, indicating that the flux densities of the two components have become more unequal. This is very similar to the behaviour of the superluminal source 3C345 reported by Cohen *et al.*²⁰; however, in the case of 3C179, the model parameters and total flux densities given in Table 1 indicate that the stronger component has increased, whereas in 3C345 it is the weaker component which decreases or perhaps becomes more diffuse and complex^{20,21}.

At both epochs the individual components each seem to be resolved and it is unclear from the models which of the components could be identified with the core and the jet usually mentioned in the context of radio source milli arc second structure. There are strong indications from the closure phase, however, that the stronger (east) component is more compact than the weaker (west) component, and thus corresponds to the core.

Pearson *et al.*⁷'s hybrid maps of the strong source 3C273 clearly demonstrate the superluminal motion of one of its components. Although this technique is unsuitable for the present observations of 3C179 because of the relatively poor sensitivity on many of the inter-American baselines, the following checks indicate that the gaussian model well represents the real source structure:

- (1) The r.m.s. residuals from the model fit are in close agreement with those expected due to random noise and small ($\sim 3\%$) calibration uncertainties.
- (2) Attempts to force a fit at either epoch with the mean angular separation of 1.16 m arcs, and allowing component sizes and fluxes to change, fail to produce a good fit to the data.
- (3) The closure phase²², where it exists, is in excellent agreement with that predicted from the models.
- (4) Separately model fitting the individual baselines independently gives the separations quoted in Table 1 at each epoch.

Discussion

It is interesting to compare the observed behaviour of 3C179 with the various models previously proposed to account for the phenomenon. However, many of the observational tests for distinguishing between models require more than two observing epochs. For 3C179 the two epochs indicate a superluminal expansion rather than contraction and it is the fifth source where this is true. (Random brightening of stationary components, as proposed by Dent²³, would predict an equal number of contractions). The magnetic dipole model²⁴ requires a separation velocity $> 4.4c$; on the basis of the cosmological parameters adopted, this condition is satisfied by the present observations.

Two further explanations of the superluminal effect require intrinsically improbable circumstances which, however, are preferentially selected when compact sources with strong radio emission are observed. In the gravitational lens model²⁵ a foreground galaxy magnifies a subluminal motion in the quasar; angular magnification makes the motion superluminal and flux density magnification makes the source bright. The compact core in 3C179 is much weaker than those of the previously known superluminal sources and thus the preferential selection

Table 1 Model parameters

Epoch	Single dish flux (mJy)	Component	Flux (mJy)	Separation (m arc s)	PA (deg)	Major axis size (m arc s)	Minor axis Major axis	PA (deg)
October 1979	670 ± 15	W	114 ± 5	—	—	0.34 ± 0.05	0.2 ± 0.1	95 ± 5
		E	209 ± 8	1.07 ± 0.01	92 ± 1	0.24 ± 0.05	0.0 ± 0.1	88 ± 5
December 1980	720 ± 15	W	107 ± 5	—	—	0.32 ± 0.05	0.3 ± 0.1	82 ± 5
		E	240 ± 8	1.24 ± 0.01	92 ± 1	0.18 ± 0.05	0.0 ± 0.1	78 ± 5

cannot be operating so strongly, unless central components of double-lobed sources are intrinsically weaker.

The most widely discussed explanation involves relativistic motion of the radio emitting regions in the superluminal sources. In the relativistic jet model, for example^{11,26}, the superluminal effect arises from the time delay between the two components when the angle, θ , of the motion to the line of sight is small. The relativistic motion towards the observer has the additional effect of enhancing the measured flux density by relativistic Doppler boosting (see ref. 27). This model has two essential elements: the Lorentz factor, γ , of the relativistic motion must be $\geq$ the apparent velocity/ c and for the minimum value of γ (in this case $\gamma = 7.6$) the angle, θ , to the line of sight must be $\sim 1/\gamma$ ($\theta \approx 7.5^\circ$).

As there seems to be good alignment between the position angle of the structure of central components and that of the outer lobes, one might assume that the entire source axis is inclined at this small angle, making the true, deprojected angular size ~ 107 arc s. This is rather large for a quasar at this redshift (see ref. 28) and corresponds to a linear size of ~ 1 Mpc; this is not, however, compelling evidence against such a small angle.

A more serious objection arises from the enhancement of flux density associated with high γ and small θ . 3C179 was chosen from a sample of 30 quasars with large (≥ 10 arc s) structure. Although the selection of 3C179 from the sample is biased towards a high γ and small θ , the sample of 30 sources is not biased towards small θ , because the outer lobe flux densities, which dominate in these sources, have been shown to be 'unbeamed'^{29,30}. Thus it is unlikely, *a priori*, that a source with the required small angle ($P \sim 0.009$) exists in the sample with the

required value of γ unless $\gamma \sim 7.6$ is typical for the sample. (This argument is independent of any alignment of inner and outer structures). Scheuer and Readhead's prediction of a lack of superluminal motion in such sources is based on their assertion that the typical γ can be no more than ~ 2 in such double sources because the observed range of boosting factors in central components is low. If this argument is correct, 3C179 must be regarded as a freak within the sample, with γ and θ conveniently contrived for the observation of the superluminal effect.

Because relativistic motion has been used to explain the rapid flux density variations in compact sources³¹, and relativistic jets can account for the efficient transfer of energy from the nucleus to the outer lobes (see ref. 32) and other morphological aspects of radio sources^{33,34}, there are reasons for retaining the idea of relativistic motions in compact radio sources. One way to ease the problem is to adopt a rather higher value of the Hubble constant. With $H_0 = 100$ the required γ becomes ~ 4.2 , $\theta \sim 14^\circ$ and overall size ~ 300 kpc for 3C179. However, the detection of superluminal motion in the first source of the type predicted not to show it suggests that the effect may be very much more common than at present thought.

I thank Dr Guy Pooley for a map of 3C179 from the Cambridge 5 km telescope and many colleagues, especially Drs Ivan Pauliny-Toth and Peter Strittmatter, for helpful discussions. Dr Arno Witzel supplied the 22.7 GHz flux density measurement. I thank the staff at the Green Bank, Haystack and Owens Valley observatories and the Bonn VLBI processor for their assistance. NRAO is operated by Associated Universities Inc., under contract with NSF.

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Non-tandem arrangement and divergent transcription of chicken histone genes

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We have located chicken histone genes within 14-kilobase pair inserts of two genomic clones, λ CH-01 and λ CH-02. The genes were mapped with chicken histone cDNA and gene-specific probes, and the identity and polarity of each gene confirmed by DNA sequencing. As previously indicated, histone mRNAs are transcribed from both DNA strands. The gene organization differs in the two clones. Although there is some clustering of genes, no repeating unit is observed. λ CH-01 contains all core histone genes, but two copies of H2A occur before the full complement of histone genes is represented. λ CH-02 contains no H4 or H2A genes, but notably has two adjacent H3 genes which are divergently transcribed. H2A, H2B and H3 genes all appear more than once in the combined inserts of the two clones, but in no case do they occur in equivalent environments. This indicates a considerable degree of disorder of the histone genes in the chicken genome.

HISTONES comprise a small group of basic proteins whose primary function is in forming the structural matrix of nucleosomes (for review see ref. 1). The amino acid sequences of histones exhibit only a narrow spectrum of divergence through

evolutionary time, consistent with their structural role in the ubiquitous nucleosome particle. In addition, species- and tissue-specific histone subtypes have been widely observed and these are regulated during embryogenesis and spermatogenesis

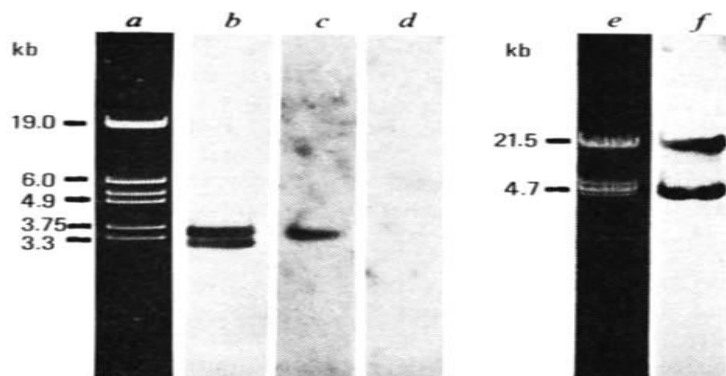


Fig. 1 Hybridization of 'histone' cDNA and specific gene probes to λ CH-01 and λ CH-02. Restriction digests of λ CH-01 and λ CH-02 DNA were electrophoresed in 1% agarose slab gels and the DNA transferred to nitrocellulose sheets^{28,29}. The filters in tracks c, d, e and f were hybridized with ³²P-DNA probes labelled by nick translation³⁰. ³²P-cDNA (tracks b, h) was reverse-transcribed from 5-day embryo 7–11S RNA¹⁷, using the random priming method³¹. The sea urchin H3 and H4 probes were constructed from fragments of the sea urchin histone gene clone h22³² cloned into pBR322. Although the H3 probe also contains a fragment of the H2B gene, track d shows that this does not hybridize to the chicken H2B gene. The chicken H2A probe was the *XhoI*–*XhoI* fragment of pCH3.3E (see Fig. 2a, fragment D), resolved on polyacrylamide slab gels and eluted as for DNA sequencing³³. a, A *Hind3*–*EcoRI* digest of λ CH-01 viewed by UV illumination of an ethidium bromide-stained gel. Sizes were determined by reference to *Hind3*-digested λ DNA run in the same gel. b, c, d, Hybridization to this λ CH-01 digest with histone cDNA, sea urchin H4 probe and sea urchin H3 probe, respectively. e, A *Sma*–*Hind3* digest of λ CH-01. f, Hybridization to this digest with the chicken H2A probe. g, An *EcoRI* digest of λ CH-02 visualized ethidium bromide-stained fragments. h, Hybridization of this digest with histone cDNA.

(reviewed in ref. 2). The amino acid changes which specify each subtype often occur in the otherwise conserved globular domains. These changes, and a variety of post-synthetic modifications^{2,3}, may alter nucleosome structure and function. It has been suggested that subtype switching is intimately related to chromatin remodelling during development of new cell types^{4,5}. The interaction of histones with both cell cycle and developmental events implies that their expressional requirements may be complex. Superimposed on this, the structure of the nucleosome dictates the need for strictly equimolar amounts of 'core' histones, and approximately half molar amounts of the

H1 group⁶. These requirements have provoked much interest in the structure and evolution of histone genes.

The highly reiterated 'early' histone genes from several species of sea urchin have been extensively characterized (for review see ref. 7). A repeating unit containing one each of the five histone genes is reiterated in tandem along the chromosome. Some histone variants are encoded in the DNA of less frequent repeats⁸. Selective expression of different repeat units has been observed, accounting for the appearance of variant histone proteins at specific stages of sea urchin development^{9,10}. It has been recently shown that individual histone gene 'orphons' are also present in sea urchin DNA¹¹.

The histone genes of *Drosophila* are organized into a compact repeat unit containing all five genes¹², but both gene order and relative gene polarity differ from the sea urchin arrangement. In *Xenopus*, histone genes are clustered and tandem arrangement is observed^{13,14}. Nevertheless, preliminary examination of two clones shows that gene order may vary^{13,14}. In yeast¹⁵ the genes for the H2A and H2B proteins are linked and transcribed in a divergent fashion. They are represented only twice in the yeast haploid genome and the two H2A/H2B pairs are spatially distinct from one another and also from the H3 and H4 histone genes.

We have previously reported the isolation of a genomic chicken histone clone, λ CH-01¹⁶. Here, we locate and orient core histone genes in this clone and extend the analysis to a non-overlapping clone λ CH-02. There is no indication of tandemly repeated genes in these inserts, and the data indicate a lack of order of chicken histone genes.

Coding potential of λ CH-01 and λ CH-02

Coding regions were located in each unit by hybridization of restriction digests of the whole clone with 'histone' cDNA, and all cDNA-positive regions were subsequently shown to contain core histone-coding regions by DNA sequence analysis. Although the embryonic RNA from which the cDNA was transcribed translates into the five histone proteins in the wheat-germ cell-free system¹⁷, it is possible that embryonic cDNA does not detect tissue-specific H1 gene variants¹³.

Two major coding regions were identified within a *Hind3*–*EcoRI* digest of λ CH-01 (Fig. 1a, b and ref. 16). These two fragments of 3.3 and 3.75 kilobase pairs (kbp) were ligated into the plasmid vector pBR325 to generate the subclones pCH3.3E

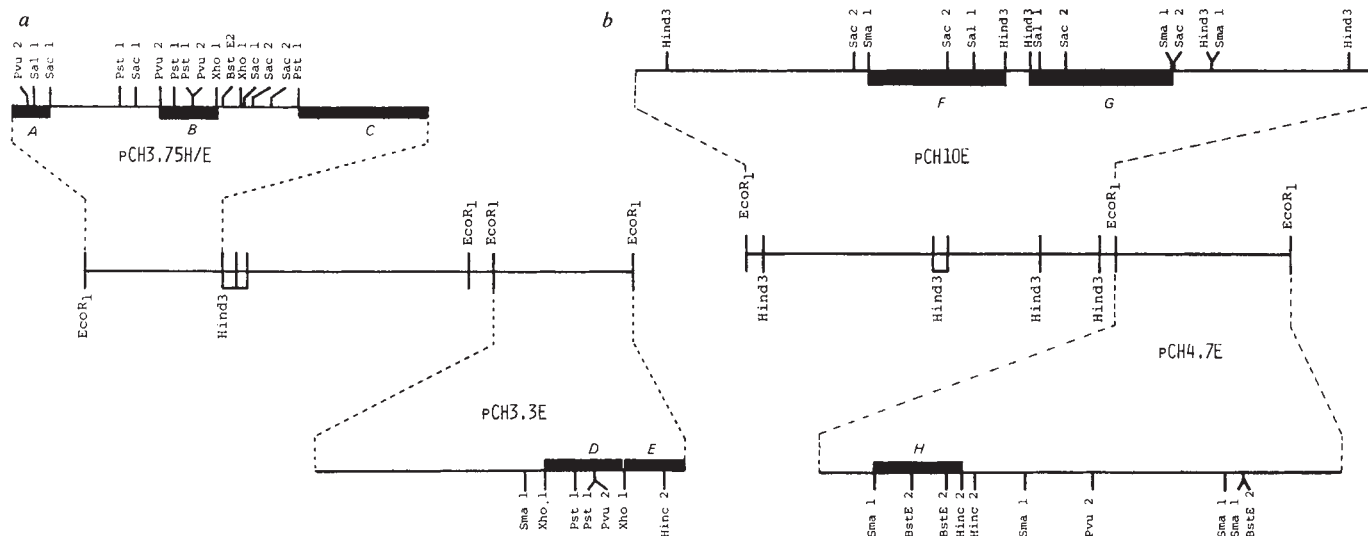


Fig. 2 Restriction endonuclease maps of λ CH-01, λ CH-02 and subclones derived from them. Blocked-in regions indicate fragments which hybridized with histone cDNA. Combinations of restriction enzyme digests were used to compile the data from the plasmid subclones and only those sites are shown which were of practical use in precise location and subsequent DNA sequence analysis of individual genes (see Figs 3–5). The insert size of λ CH-01 is 14 kbp and that of λ CH-02 14.7 kbp. All maps of the subclones except pCH10E have been enlarged three times relative to the overall λ CH-01 or λ CH-02 maps. The size of pCH10E has doubled relative to λ CH-02. The position of the small *EcoRI* fragment of λ CH-01 is corrected here from its previous allocation¹⁶. a, cDNA-positive regions A, B, C, D, E of λ CH-01 subclones pCH3.75H/E and pCH3.3E, respectively. b, cDNA-positive regions F, G, H of λ CH-02 subclones pCH10E and pCH4.7E, respectively. These regions are referred to in the text and are subsequently identified by DNA sequence analysis (Figs 3, 4).

and pCH3.75H/E, respectively. The subclones were mapped with restriction endonucleases and coding regions were located in finer detail using histone cDNA (Fig. 2a). Five coding regions (A-E) were identified, suggesting that λ CH-01 encoded multiple genes.

A similar analysis of λ CH-02 revealed coding regions within both the 10- and 4.7-kbp *Eco*RI fragments (Fig. 1g, h). These were subcloned (pCH10E and pCH4.7E) and further mapping and cDNA hybridization studies revealed three coding regions, F-H (Fig. 2b).

Detection of genes in CH-01 using specific coding probes

To identify the coding regions indicated in Fig. 2a, we screened λ CH-01 with specific gene probes. Due to the conservation of histone amino acid sequences through evolution, sea urchin probes have proved useful for detecting histone genes of other species¹². Our own findings suggest, however, that these cross-species probes must be used with caution. Although the H4 sea urchin probe showed specific hybridization to chicken recombinants, the sea urchin H3 probe and a probe containing a fragment of the *Drosophila* H2B gene gave ambiguous hybridization results when used on λ CH-01. Similarly, results from this laboratory indicate that the sea urchin H3 gene probe does not cross-hybridize unambiguously with an authentic human H3 histone gene. These observations question the results of previous attempts to detect histone gene transcripts in mammalian cells^{18,19} using sea urchin probes.

The presence of an H2A gene in λ CH-01 has been previously recognized from DNA sequencing¹⁶. This was unambiguously located in pCH3.3E (Fig. 2a, region D) from the position of restriction sites. An H2A gene-containing fragment bounded by *Xho*I sites (Fig. 2a, region D) was excised and used as probe to re-screen λ CH-01. The sea urchin H4 probe and the homologous H2A probe hybridized to λ CH-01 (Fig. 1c and f, respectively). No hybridization was observed with the sea urchin H3 probe (Fig. 1d). The H2A probe hybridized to two distinct regions (Fig. 1f), indicating the possibility that λ CH-01 contained two H2A genes.

H3 and H2B genes identified in cDNA-positive regions of λ CH-01 and λ CH-02

As noted above, H3 and H2B heterologous probes were unsatisfactory for detailed analysis of the chicken histone clone λ CH-01. Fine hybridization mapping of the subclones pCH3.75H/E and pCH3.3E indicated two cDNA-positive regions, A and E (Fig. 2a), that did not hybridize with the available cross-species probes. Direct DNA sequence analysis identified these regions as H3 and H2B genes, respectively (Fig. 3).

The genomic clone λ CH-02 was originally identified as a histone gene clone on the basis of hybridization with a histone cDNA probe (ref. 1 and Fig. 2b). It did not hybridize with heterologous H2B or H4 probes (data not shown); however, the cDNA-positive regions F, G and H (Fig. 2b) did hybridize with H3 and H2B coding regions derived from λ CH-01. DNA sequence analysis of these regions showed that regions F and G of λ CH-02 contain adjacent H3 genes and that region H contains an H2B gene.

Thus, all cDNA-positive regions of λ CH-01 and λ CH-02 were shown to contain chicken histone genes. Portions of the nucleotide sequences which serve to identify each of these genes are shown in Fig. 3.

Location and orientation of histone genes

The precise location and orientation of all the core histone genes in λ CH-01 and λ CH-02 may be deduced from restriction enzyme mapping and DNA sequence analysis (Figs 2, 4). All core histone coding regions present in λ CH-01, except for one region in an H2A gene, have been fully sequenced (Fig. 4). In each case the nucleotide sequence predicts the expected amino

H3	
pCH3.75H/E	*(A) ATG GCG CGT ACG AAG CAG ACG GCG CAT AAG TCG
pCH10E	*(F) ATG GCG CGT ACG AAG CAG ACG GCG CGT AAG TCG
pCH10E	*(G) ATG GCG CGT ACG AAG CAG ACG GCG CGT AAG TCG
	ala arg thr lys gln thr ala arg lys ser
CHICKEN H3	ala ¹ arg thr lys gln thr ala arg lys ser ¹⁰
H2A	
pCH3.75H/E	*(B) ATG TCG GGG CGC GGG AAG CAG GGC GGG AAG GCG
pCH3.3E	*(D) ATG TCG GGG CGC GGA AAG CAG GGC GGG AAG GCG
	ser gly arg gly lys gln gly gly lys ala
CHICKEN H2A	ser ¹ gly arg gly lys gln gly gly lys ala ¹⁰
H4	
pCH3.75H/E	*(C) ATG TCT GGC AGA GGC AAG GGC GGG AAG GGC CTC
	ser gly arg gly lys gly gly lys gly leu
CALF H4	ser ¹ gly arg gly lys gly gly lys gly leu ¹⁰
H2B	
pCH3.3E	*(E) ATG CCC GAG CCG GCT AAG TCC GCG CCC GCC CCG
pCH4.7E	*(H) ATG CCT GAG CCG GCC AAG TCC GCA CCC GCC CCC
	pro glu pro ala lys ser ala pro ala pro
CALF H2B	pro ¹ glu pro ala lys ser ala pro ala pro ¹⁰

Fig. 3 Identification of histone genes in λ CH-01 and λ CH-02 by DNA sequence analysis. DNA sequences of all genes except the H2B gene in pCH4.7E were determined by the methods of Maxam and Gilbert²³. Sequences from this gene were obtained by the methods of Sanger and Coulson²⁴. The nucleotide sequences shown cover a region coding for the first 10 amino acids of each protein. The amino acid sequence for chicken H4 and H2B are not known. The genes for these proteins were assigned by comparing the amino acid sequences predicted in one reading frame with the respective calf amino acid sequences. The identifying DNA sequences are given in the order A to E and F to H shown as cDNA-positive regions of λ CH-01 and λ CH-02, respectively, in Fig. 2a and b. The extent to which nucleotide sequences have been determined in each coding region is shown in Fig. 4.

acid sequence for the respective histone protein. There are no intervening sequences or frameshift mutations and thus the genes located within λ CH-01 are not pseudogenes. The limited nucleotide sequence data for the H3 and H2B coding regions in λ CH-02 so far predict amino acid sequences expected for these two histones. The notable feature of λ CH-02 is the presence of adjacent, divergently transcribed H3 genes, separated by about 0.8 kbp of DNA. Although the H2A/H2B and H3/H4 gene pairs of yeast¹⁵ and *Drosophila*¹² are divergently transcribed, this kind of organization for a histone gene pair coding for the same protein has not been described previously. The significance of the H3 gene pair disposition in the chicken system is unclear. By extrapolation from the recently described chorion gene system²⁰, it is possible that the organization of divergently transcribed genes is significant for the expression of tissue-specific variants.

The overall arrangement of core histone genes within λ CH-01 and λ CH-02 is shown in Fig. 5a and b, respectively. The two inserts are non-overlapping and although some clustering of genes occurs, there is no obvious tandem repeating unit. Within λ CH-01, the H2A gene appears twice before a full complement of core histone genes is represented. The tightly linked H2A/H2B gene pair seen in λ CH-01 is not present in λ CH-02 and the adjacent H3 genes in λ CH-02 are not related in an organizational sense to the H3 gene in λ CH-01. In other words, no two genes coding for the same histone are in equivalent environments. (These results refute our previous indication of a 15-kbp repeat for chicken histone genes using uncloned probes¹⁷ and are consistent with preliminary analyses of other chicken histone clones²¹.) The clones also contain long stretches of non-histone DNA. For example, in λ CH-01, 9 kbp of DNA separate the H4 gene from the distal H2A gene (Fig. 5a) and an inter-gene distance of 4 kbp is seen in λ CH-02 (Fig. 5b).

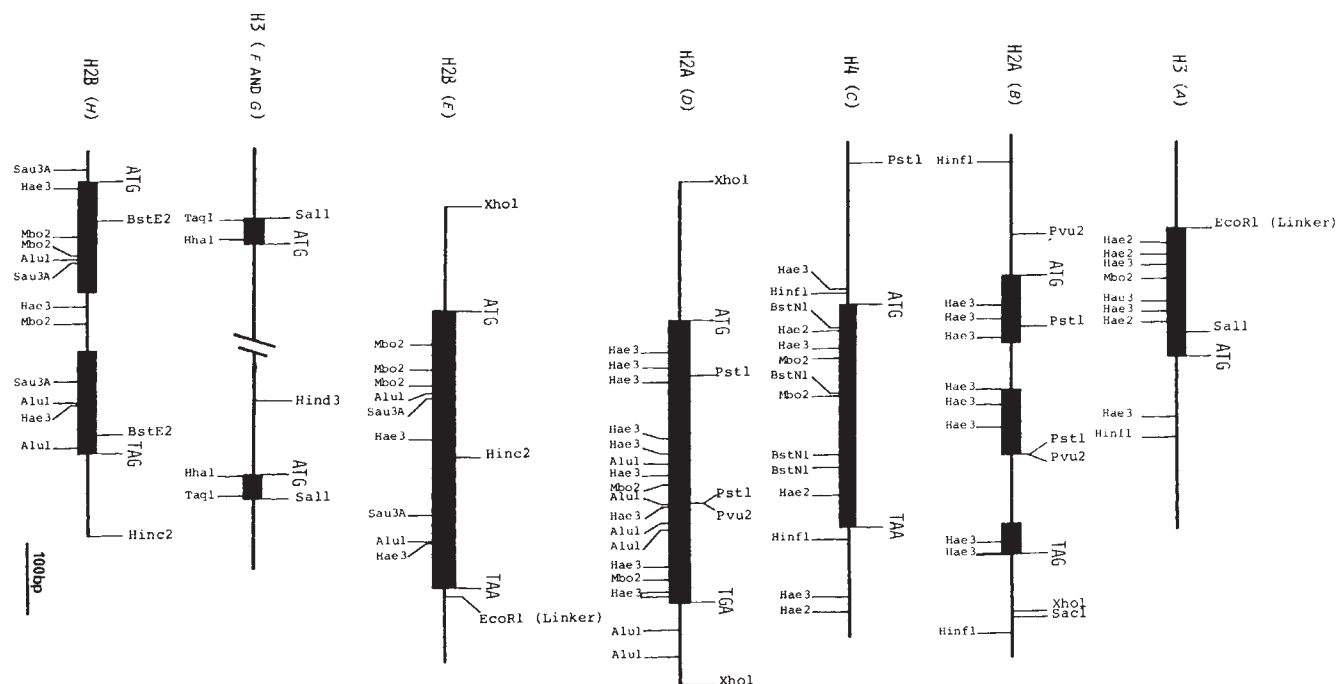


Fig. 4 The coding regions of genes in λ CH-01 and λ CH-02. Initiation and termination codon sites are shown for each gene where known. Restriction sites above the line can be used to orient the genes (see also Fig. 2). The blocked areas indicate coding regions for which the nucleotide sequence has been determined. Each gene fragment is identified A to H relative to the cDNA coding regions indicated in Fig. 2.

The relative disorder of histone genes in chicken may contribute to an understanding of histone gene evolution. The histones themselves represent highly conserved proteins with a defined function and it is unlikely that the mode of expression of histone genes would have changed dramatically through evolution. Preliminary data on a human histone gene clone (ref. 22 and unpublished data) suggest that marked histone gene disorder may also occur in other vertebrates. Although histone genes are frequently organized into ordered repeating units, there is little to suggest that this is a requirement for expression. The relative disorder of chicken histone genes also suggests that they are independently controlled. An explanation is therefore required to account for the evolution of histone genes from an ordered to a disordered disposition. It is possible that the concerted evolution of histone gene clusters in invertebrates is a function of chromosomal correction mechanisms acting on reiterated genes²³⁻²⁷, and that non-concerted evolution of chicken histone genes has arisen because the vertebrate gene copy

number is low⁷ and correctional recombination events are less frequent. In this view, the gene organization in chickens is a remnant of the ordered arrangement of invertebrates, conserved in these species because they are more highly reiterated and not because of a functional requirement.

Clustering of histone genes in tandem arrays as first described for invertebrate systems remains the predominant histone gene organization in those species studied so far. Variations are seen in sea urchin orphans¹¹, yeast¹⁵ and *Xenopus*^{13,14}. More recent data confirm that the major histone gene unit in *Xenopus* is a 14-kbp clustered array^{13,14} and that the variants λ Xlh4 (ref. 13) and XI-hi-1 (ref. 14) may be 'orphan like'. Unequal recombination events could result in the appearance of isolated genes or groups of genes, and these elements might be expected to show extensive population polymorphism as is indeed the case for sea urchin histone gene orphans¹¹ and the minor histone gene components of *Xenopus*¹⁴. It is unlikely that the chicken histone genes analysed here represent orphans. Southern blot analysis (ref. 21 and our unpublished data) is not consistent with the existence of a major repeating histone gene cluster in the chicken genome.

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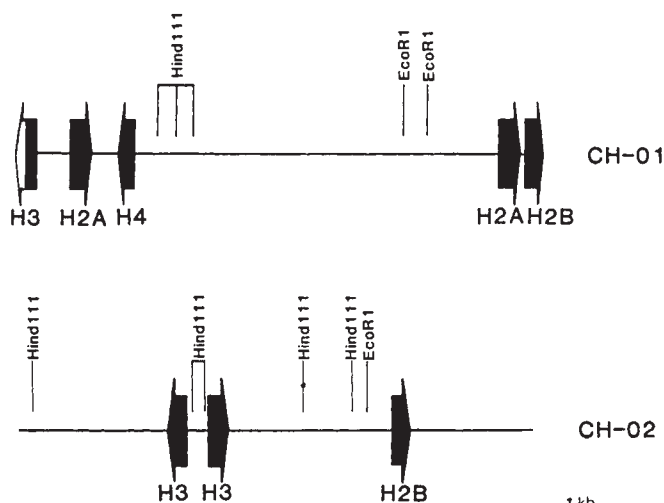


Fig. 5 Location and orientation of chicken histone genes. The precise location and orientation of genes in the two clones λ CH-01 and λ CH-02 relative to *EcoRI* and *HindIII* restriction sites are indicated.

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Sequence homologies near the C-termini of the variable surface glycoproteins of *Trypanosoma brucei*

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African trypanosomes evade their mammalian host's immune system by the sequential expression of alternative surface glycoproteins. Comparison of the cDNA sequences of five antigenically distinct surface proteins and the C-terminal amino acid sequences of four additional ones demonstrates that these nine glycoproteins can be classified into two subsets based on C-terminal amino acid homologies that extend 75–105 amino acids into the protein.

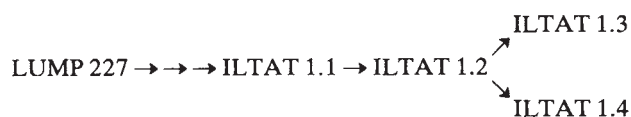
UNICELLULAR parasites of the genus *Trypanosoma* cause extensive disease in both humans and livestock¹. In Africa the disease is especially widespread among domestic livestock and thus severely limits the consumption of meat and milk products by over 200 million people living south of the Sahara Desert². The parasite resides in the bloodstream of its mammalian host and appears to evade the host's immune response by sequentially expressing a series of different surface glycoproteins, the variable surface glycoproteins (VSGs)^{3,4}. The largest documented number of immunologically distinct VSGs that can arise from a single trypanosome clone is 101, reported for *Trypanosoma equiperdum*⁵; the maximum potential number is unknown.

VSGs isolated from *Trypanosoma brucei* are best characterized. The VSGs constitute at least 95% of the surface protein of this organism and as much as 10% of the total cell proteins⁶. *T. brucei* VSGs have molecular weights between 55,000 and 65,000 and most of those studied have widely different amino acid compositions, dissimilar peptide maps, different isoelectric points and variable carbohydrate content^{7–11}. In addition, the N-terminal sequences of 15–30 amino acids reported for five different VSGs are very different and have no obvious relationship^{3,9}. Nevertheless the different VSGs do have a similar biological function. They comprise a cloud or shell that shields other membrane proteins from the host's immune system. As such, each collection of unique VSGs must be able to assume a uniform and closely ordered array on the surface of the organism.

Here we compare five different VSG cDNA sequences and, together with the C-terminal amino acid sequences of four others, demonstrate that the VSGs characterized so far can be grouped into two major subsets based on amino acid homologies near the C-terminus.

Origin of the VSG cDNAs

The ILTAT series of *T. brucei* clones are derived from LUMP 227¹², which originated from a trypanosome stock isolated in 1964 from a cow in Kenya¹³. They are serially related as follows.



In each case the ILTAT clone was isolated from the first

trypanosome relapse population in an experimental animal infected with the previous clone: for example, ILTATs 1.3 and 1.4 were each isolated from a laboratory mouse infected with ILTAT 1.2. The construction, identification and initial characterization of the four ILTAT VSG cDNAs are described elsewhere^{14–17}.

The partial sequence of VSG 117 cDNA, shown in Fig. 1, was recently reported by Boothroyd *et al.*¹⁸. Trypanosome clone 117 is derived from another *T. brucei* stock isolated in 1960 from a sheep in Uganda¹⁹.

VSG nucleotide coding sequence homologies

Nucleotide sequences of VSG cDNAs of ILTAT 1.2, ILTAT 1.3 and 117 are compared in Fig. 1; the sequences of ILTAT 1.1 and 1.4 cDNAs are compared in Fig. 2. No direct amino acid sequence information is available on the ILTAT VSGs. However, the amino acid sequences of each can be deduced from the nucleotide sequences as each contains only one large translation reading frame uninterrupted by termination codons. The largest cDNA, ILTAT 1.3, extends 1,515 nucleotides from the 5' end of the cDNA to the (DNA) termination codon TAA, followed by 87 nucleotides (including three additional termination codons in phase) before the poly(A) region is reached. The corresponding protein of 505 amino acids has a molecular weight (MW) of 54,886, which is within the range of native VSGs, if adjusted for the addition of carbohydrate moieties and the potential proteolytic processing of an N-terminal signal sequence²⁰ and the hydrophobic portion of the C-terminus¹⁸. Unfortunately there is no definitive way to determine from the nucleotide sequence alone whether one of the two methionine codons near the start of the ILTAT 1.3 coding sequence is the translation initiation codon. The 16 hydrophobic amino acids that immediately follow the second of these methionine residues possibly represents an N-terminal signal peptide although there is no experimental evidence for this conclusion. The other cDNAs are smaller and do not contain the entire VSG coding sequence.

Comparison of the nucleotide sequences in Figs 1 and 2 reveals striking homologies among VSG coding sequences previously thought to be unrelated based on nucleic acid hybridization studies²¹, N-terminal amino acid analyses³, and antibody cross-reactivity^{6,12}. In Fig. 1, the sequences of ILTAT 1.3 and 117 cDNAs were initially compared by aligning the termination codons of their open translation reading frames. The ILTAT 1.2

90
1.3 CAG AAA ATG ACT AAA GCG TAC GAA AAT CCG ATG CTT CTG CAG GCT CTC GTT TTA GCC GCG GTA CTC TGC ACA ACC CAT GCC GAA GGA ACC

180
1.3 GCG AAA GCG CCT TTA AAG CAC AGT GTT GCA ACG GGG TTC TGT TCA TTC TCA AAA GCC GCA AAA CAA GCA GCA AAC AAA CTA GCG CAA ACC

270
1.3 TTG GAT GCG GTT AAG GCC ACC TTA AAT CAG AAC AGA AAA GCA CAT CTA CAG AAT TTA CTG GTA GCG GTG AAG AGG CCA ACT GAG CAA ATA

360
1.3 GCT GCG CTA ATA CTG GGG CAA TAT GCA AAC ACG CAG GCG GCA AGC GGC CTT TCA GAC CTC GGC AAG TGG GCA CCA GAC GAA ACA AAG ACA

450
1.2 ATT GGC CAG GCG CTA TAC ACA AGT GGG CGG CTA GAC GGT TTC ATA GAC GTT TTG GAC GGT CAC CGT TCA GAA AAC TCG GGC CAG AAC AAA
1.3

540
1.2 AAC AGC GGT TAC TAC CAG GCA AAG AAA CTG CAA GGA GAA GAC ACA GAA TGC GAT CTG GAA CCA CAC GAG CTA AAA CTA TCG CCA CTC
1.3 AAC TGC ATC GCC AAC GAC GGC GAG GGG ACG AAG GCT TTC GAC TTC GAT CTG TGG GGG CCC AAC GCA GCA AAA GCG GGA AAC

630
1.2 GAA ATA GAA GTC ACA GAC GCC GAC GGC TTC ACA AAG GGC CTG GCA CCC GGC GTA GCA GAC TCT CAC CAA ACT CAA GGC ACC AAA GAA TGC
1.3 GAA CCC GGA GAC CTT AAA AGC TCT GAT GAA AAG AAG GGC TTT TGG TGG CAT CGG GCG GCA GCA GCA AGC GGC GGC AAT AAC CAC TGT GTA ATT

720
1.2 GGT CTG TTA ACA CTT CAC GGG AAC AAT GGG CTA GCG AAG TCG GGT GGC CTT GAC CAG AAC CCC AAG CTT TTA ATG GGA GTC TTC ACG GTC
1.3 TTC GAC GAC CTC AAT ACA GCA TAC TCA ACA AAG ACA GCA GCC ACA GAC TTT CTC GGC GGA CTC ATA AAG GTC CAC CAA ACA ACC GGG CTG

810
1.2 GCC AGC AGC AAC AGC GCA CTA ACA GTA GCC GAC CTC ACT AAG GCC GCG ACG TCG GCA ATC GCA AAT ACC GGC CTG GGC CAA GCA CAC GCC
1.3 ACA GCG GCA ACG GCG ATT GCG GCG CAA AAG AGC ACA AAT AAA ATT CTA AAA GAC ATC GAC GCC AAC TGG CCA AAA GTT CAG CAG GCA TAC

900
1.2 GCA GTC AAG GCG ATT CAG GAC GCC AAC CCG GCC GCA AAT GAC AAT ACA TCA ACA TCA GAA GAT ACG GCA GAA CTC CAA ACG GCA ATC ATG
1.3 ACA ACA GCA GCA GGA AGA AGC CCG ACG ACG GAA CAG GAA TAC AAA GAT CTA CTA AAA GAC GAA AGC AGT AGG CAA AAA CTT CGC GCA GCA

990
1.2 CAC CTA GAA CTG CAG GCC GGC ACC GCA GCG AGC CGG AAC ATG AAA GAG GAA ACA AAA ATA TTC ACG AAC AAA GTA CAA GAC ACC ATC
1.3 GCG CAA ACG GTG AAC AAC TGG AAA CCA GCA GAC AAA CCT GCA AAC ATG GAC GAT TAC CTC AAG CAG GTA TTT AAA ATA GAC GCA AAT GTC

1080
1.2 ACC AAG GTA CTG CAC AAT GTG TAC AGT CAC CAA ATC ACC GTC CCA TTT GTC AAT AAC GGC AAG GAC ACT CCC CTA CGG AGC ATA CCA AAC
1.3 AAT TCA GCG TAC GTA ACA GCC ATG AAG AAG ATA AGT ATG GAT GTG CCA ACA AAG GAT GGT GAA ACC CAA AAG AAG GAG CTA TTC GAG ATG

1170
1.2 ACA GGA GAA CTG ATG GAA ATC TTA GCG TTC TAT GAA CAA AAG GTC GCA GAT AAC ACA GCG AAG ACA CAA AAA GAA CTA ACG GAG GCA CAG
1.3 TCT GAA GAG GAC CTA GAA GCA GCC CTA GCA GTG GAA ATT AGA GCA TTA TCA AGC GAA AAT GCA AAG CTT ACC ACA GAA GTG AAG CAA CTC
GAA ACC GAA

1260
1.2 CAG GCA ATG AAG ACA GAC AGA AGT GGC GAC GCG GAC TGC ATT GAA ATC AAG GAA CCG ACG GCA TGC AAC AAG AAA CCT TTT TGC AGT TAT
1.3 AGA CCA AAT CAA GGT AAA CAG GGT ACG GAA GAC ACG TGC AAG AAA ATG AAG GAT GAA ACG GCG TGC AAC AAC AAG CCT TTT TGC ACC TAT
117 CTA GCA GAT CAA AAA GGC AAA TTT CCT GAA GCG GAG TGC AAT AAA ATA TTT GAG GAA TCT AAG TGC AAC GGC GGC AAG ATA TGC AGT TGG

1350
1.2 AAT GAA AGC ACA ACT GAT GAA GAA AAG TGC AAA TTT AAT GCG ACA AAA GGT GCA GAA AAT GGA GTC GCT GTA GCA CAA ACT CAA ACT
1.3 AAT GAA AGC ACA ACT GAT GAA GAA AAG TGC AAA TTT AAT GCG ACA AAA GGT GCA GAA AAT GGA GTC GCT GTA GCA CAA ACT CAA ACT
117 GAT AGC GAG GAT GAA GCG GAA GAA AAG TGC AAA TTT AAT GCG ACA AAA GGT GCA GAA AAT GGA GTC GCT GTA GCA CAA ACT CAA ACT

1440
1.2 GGA GGG AGT GAA ACA ACA ACA GAG AAA (C)
1.3 GGA GGA ACG GAA ACA ACA ACA GAT AAA TGC AAA GAT AAG AAA GAT GAC TGC AAA TCT CCG GAT TGT AAG TGG GAG GGC GAA
117 GCA GGA ACG GAA ACA ACA ACA GAT AAA TGC AAA GAG AAT TGG GAA GAT ACG TGC AAG AAG GCG AGC AAC TGC AAG TGG GAA AAT AAT

1530
1.3 TGC AAG GAT TCC AGT TTT ATT CTA AAG AAG CAA TTC GCC CTC AAG GTG GTT TCT GCT GCA TTT GCG GCC TTG CTT TTT TAA TCC CTT
117 GAT TGC AAG GAT TCC AGT TTT ATT CTA AAG AAG CAA TTC GCC CTC AAG GTG GTT TCT GCT GCA TTT GCG GCC TTG CTT TTT TAA TCC CTT

1620
1.3 TCC CTT CTT TTT CTT CCA TGC AA AAA TTC TTG CT AA AAA TTT GCT ACT TGA AAA CT TCT GAT ATA TTT TAA CA CTA AAA AAA AAA
117 TCC CTT CTT TTT CTT CCA TGC AA AAA TTC TTG CT AA AAA TTT GCT ACT TGA AAA CT TCT GAT ATA TTT TAA CA (C)₂₀

1.3 AAA AAA AAA AAA (C)₂₅

Fig. 1 Nucleotide sequences of ILTAT 1.2 and 1.3 cDNAs compared with the VSG 117 cDNA sequence as reported by Boothroyd *et al.*¹⁸. Sequence determinations were carried out using the methods of Sanger³⁰ and Maxam and Gilbert³¹. Most areas were verified two to four times by sequence overlaps. (Sequencing strategy and duplicate autoradiograms of sequencing gels are available on request.) The three sequences are aligned to maximize nucleotide homologies; this necessitated treating two different triplets in the coding region of VSG 117 as insertions relative to ILTATs 1.2 and 1.3 and four different locations in the 3' untranslated region of VSG 117 as deletions relative to ILTAT 1.3. The boxed regions indicate nucleotide homologies within the last 330 nucleotides. No significant homologies were detected before this region. The asterisk shows the termination codons. The region between the vertical bar and the asterisk codes for a 23-amino acid hydrophobic tail (see Fig. 3).

Fig. 2 Nucleotide sequences of ILTAT 1.1 and ILTAT 1.4 cDNA aligned to maximize the homology that occurs near the 3' end of ILTAT 1.4 cDNA. This necessitated treating one triplet in ILTAT 1.1 as an insertion relative to ILTAT 1.4. Sequences were determined by the method of Maxam and Gilbert³¹. Boxed regions indicate homologies within the last 100 nucleotides of ILTAT 1.4 cDNA. No significant homologies were detected before this region. The region between the vertical bar and the asterisk codes for a 17-amino acid hydrophobic tail (see Fig. 5).

1.1 GTT GCC TGC AAA AAC GGC GGC GGC GCA TGC AGT GCA GCC AGC AGC AGC GAC AAA ATA CAT ATA ACG ATC GAA ACG GAC AGC AAA AAC AAA
1.4 GT TTC TAC CAG CAC CAA ACC AAG GTA ATG CAC CTT GGC GGG TAC CTA GAA ATA ACA TCA GGA GCA GGC AGA ACG ACG

1.1 GGG ACA GCG GCC AGC ACG ATG GAC TCC CAA AAC ACA GCG GTC GCA TTC GCA ACG GAG CTG CAG ATT GGA AGC TGG AAA AGC CAG CAC ATA
1.4 CTA GAA CTG AAA AAC CTC AAC GAC ATC GCA CAG GAC GGT GTA CAC AAA AGC GGG CAG CTA TTG GGA GAG ATC TAC ACA CCG CTT GCA ACA

1.1 GAC AGC AAC ATA ACG GCT TTG GCG AAT GCC TTA ACA GCA CTA GAC AGC ATT CCT GAC CTC ACA GAC CCA ACG GCT TAC ACA GCA GAC GCG
1.4 TTA AAC AGT GAA GAC ACA ACA GAA ATT AAA ACC ACA GAT GAA AGC ATA ATA AGA AGC GCT GCA GCT GCC AGC ACA TTA GAG GCC GCC GTT

1.1 GCG TTC AAA CAA CTA GTA GCC ACA GTA GCG CTC AAC AAG CCG CCA ACC ACG GAG CTA ACC GGA GAA GTT CTA GAC GCA GTA AAA CAG AGC
1.4 CAG GAG GCT CTT AAA CTG GCA AAT CCC GAG ACG GAC CAA GAA AAG CTG AAA GAA GAA GCA GCA GAC ATC ATC AAG GAG TTT GTG GGA AGC

1.1 ATG TGC CGA CAA CTA CCG AAC CTC GGC AAG CGA GCT GAC GAC AAA ATT TGG GAA CCG TTA AAT GAA CAG ACG GCC AGC TAC TAC AGC GAA
1.4 GAA AAT ACA AAG GGT TCC AAG GCT TGG GAA AAA CTA AAG TCG ACA AAA GTG AAG GGC ACA GAG GCG AAA CCC GAA ACA GAA AAA GAG CTA

1.1 AAA ACT ATC AAA ACC GAC CAA CTA AAG CTA CTA ACA AGC AAC CAA CAG CTG ACA ACT GCA CTA GGA GTA GCA CTG GCG AAA GCA ATA AAC
1.4 AAA GAC ATT ACT CAC AAC GCT AAA CTG GTG TCG GCA CTA AAT TAC TAC ATC AGC AGT GCT GAA TCT AAG CTA CAG GAA GCG GAG ACA AAA

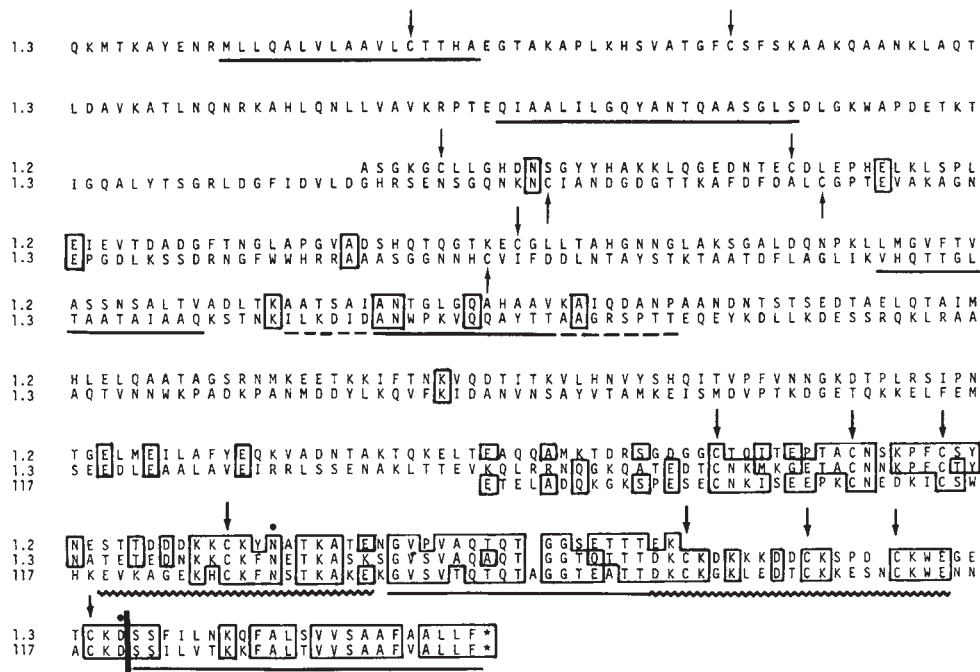
1.1 GTA AAA GAA GCT TCC AAA AAG GAA TGC AAC CTA CAC GGC CAT GAA ACA GAC GCT ACG TGC GAG GCA AAA GGA GTA GGA GAT AAG TGT AAA
1.4 CTA GCA GCA ACA AAA GCT GCA GCT GAA AAA GTG CCA ACA GCG CCT AAA CCA GAT GAA TGC AAA GCT AAA AAG GGG GAC ACC TGC AAA

1.1 CCC CCA TGC AAA GAA GTC GAA GAA GGT GGA AAA AAG AAG TGC AAA TTG GAT AAA GAG GAG GCG AAA AGG GTA GCA GAA CAA GCA GCA ACA
1.4 GAT GGA TGC AAA TGG GAT AGC GAC GGT GGA AAC AAA AAG TGC GTA TTG GAT CCG AAT TAC ACA AAA AAA (C)₂₉

1.1 AAT CAA GAA ACA GAA GGC AAA GAT GGA AAA ACC ACA AAC ACC ACA GGA AGC AAT TCT TTT GTC ATT CAT AAG GCA CCA CTT TTT CTT GCG
1.1 TTT TTG CTT TTT TAA TTT TTC CCT TTA AAA TTT TCC TCC TTT AAA AAC AAA TTT TTT CTA CTT GAA AAC TTC TGA TAT TTG ATA TAT TTT

1.1 AAC ACC TTT AAA AAA AAA AAA AA (C)₂₅

Fig. 3 Amino acid sequences of ILTAT 1.2, ILTAT 1.3 and VSG 117 as deduced from the nucleotide sequences shown in Fig. 1. The C-termini of ILTAT 1.3 and VSG 117 are indicated by an asterisk. Boxes show amino acid homologies. Horizontal and wavy lines underneath the sequences indicate hydrophobic or uncharged polar and hydrophilic regions, respectively. Broken lines indicate regions that are uncharged polar or hydrophilic in one sequence but not in the other. Arrows indicate the cysteine residues. Dots show two glycosylation sites in VSG 117²⁶. The large vertical bar indicates the proposed cleavage site of a 23-amino acid hydrophobic tail from the nascent VSG.



sequence was then aligned to maximize homology with the other two sequences. The homology among the three cDNAs starts ~330 nucleotides before the termination codon and extends through the 3' untranslated region to the poly(A) terminus at the 3' end. Based on this alignment, the ILTAT 1.2 cDNA sequence ceases ~140 nucleotides before the termination codon.

The cDNA sequences of VSG 117 and ILTAT 1.3 both contain the 3' untranslated sequence between the termination codon and the poly(A) region (although the VSG 117 sequence seems to stop two nucleotides before the poly(A) region). These two 3' untranslated regions are virtually identical except for four deletions of 1, 3, 7 and 13 nucleotides in VSG 117 (or four insertions in ILTAT 1.3). The remaining 59 nucleotides in both sequences differ at only two positions.

The ILTAT 1.1 sequence (Fig. 2) also includes the 3'-terminal poly(A) region of the mRNA. The distance from the termination codon to the poly(A) in this case is 84 nucleotides. Alignment of all three untranslated regions to maximize homology (not shown) reveals that 42 positions are identical in the three VSG mRNAs, mostly near the poly(A) end. The significance of these observations is unclear but it does seem that portions of the 3' untranslated region do not tolerate much mutational drift. Similar sequence conservation has also been observed in the 3' noncoding region of different haemagglutinin genes of influenza virus RNA²². In contrast, the different mammalian β -globin genes have a high degree of sequence divergence in this region²³.

Aside from the 3' untranslated region and the last three codons of the coding region, ILTAT 1.1 cDNA does not possess distinctive homology with the cDNAs of ILTAT 1.2, ILTAT 1.3 and VSG 117 shown in Fig. 1. However it does have similarities to ILTAT 1.4 cDNA. As aligned in Fig. 2, 61 of the last 100 nucleotides of ILTAT 1.4 are the same as the corresponding nucleotides in ILTAT 1.1. On this basis, the ILTAT 1.4 cDNA stops ~123 nucleotides before the termination codon. Therefore if this homology extends to the termination codon of ILTAT 1.4 coding sequence, it comprises ~225 nucleotides (or 75 codons).

Amino acid sequences of VSGs are conserved near the C-terminus

Figure 3 compares the deduced amino acid sequences of ILTATs 1.2, 1.3 and VSG 117. These comparisons indicate that amino acid homologies near the C-terminus parallel and extend beyond the nucleotide sequence homologies noted in Fig. 1.

Furthermore, many of the amino acid changes near the C-termini are conservative in that an amino acid of similar polarity has been substituted. Generally, the C-terminal 105 amino acids of all three VSGs are highly conserved, the next 15 positions are less conserved, and a comparison of ILTAT 1.2 and ILTAT 1.3 through the next 390 amino acids towards the N-terminus reveals no significant amino acid homology (although there may be some conservation of domains as discussed below).

Figure 4a illustrates the common features of the three sequences. Within the highly-conserved C-terminal 105 amino acids are eight cysteine residues whose relative positions in the three VSGs are constant. This feature is very similar to that of the influenza virus surface glycoprotein, haemagglutinin, which also undergoes antigenic variation and contains eight invariant cysteines in the last 100 amino acid residues²⁴. Air and Hall²⁵ have examined 35 different haemagglutinins of 17 different influenza subtypes and found that the cysteine residues are invariant throughout the entire protein. This suggests that disulphide linkages have an integral role in maintaining a general three-dimensional conformation of variants of both trypanosome VSGs and influenza haemagglutinins.

The last 23 codons of the ILTAT 1.3 and VSG 117 coding sequences specify a very hydrophobic region; seven of these amino acids are different in the two sequences but only one

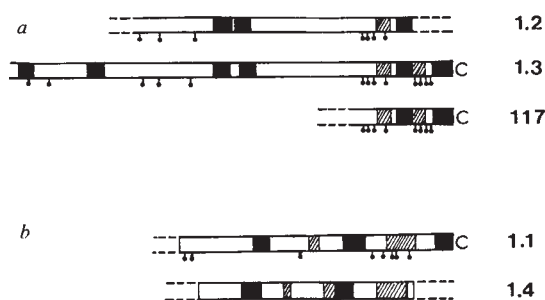


Fig. 4 Summary of the conserved features of a, ILTATs 1.2 and 1.3, and VSG 117 and b, ILTATs 1.1 and 1.4. C indicates the C-terminus; solid boxes are hydrophobic or uncharged polar regions; cross-hatching indicates highly hydrophilic regions; ↓, cysteine residues. Broken horizontal lines represent regions for which no sequence information is available.

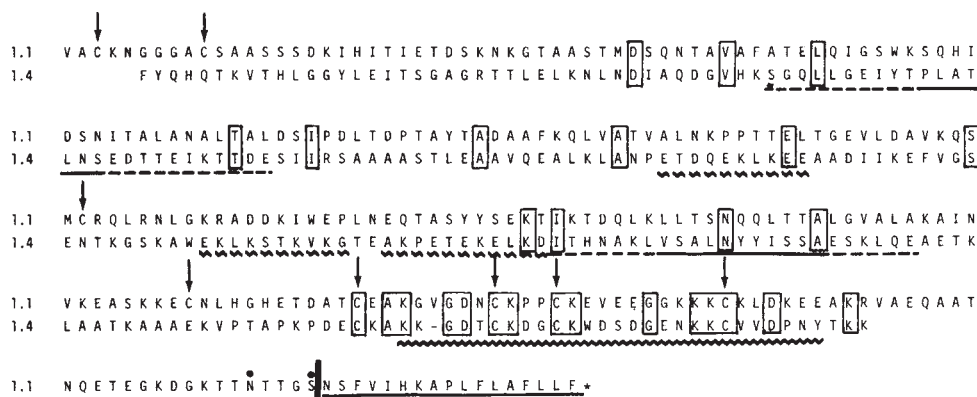


Fig. 5 Amino acid sequences of ILTAT 1.1 and ILTAT 1.4 as deduced from the nucleotide sequences shown in Fig. 2. Symbols are the same as for Fig. 3. The C-terminal hydrophobic tail in ILTAT 1.1 is 17 amino acids long.

change involves a charge difference at neutral pH. Boothroyd *et al.*¹⁸ and Holder and Cross²⁶ reported that this 23-amino acid hydrophobic sequence is not present in the mature VSG based on C-terminal amino acid analysis of VSG 117. Furthermore, they found that the C-terminal residue is glycosylated. (The cDNA sequence of both ILTAT 1.3 and VSG 117 indicates that this terminal residue is aspartic acid, which implies an unusual glycosylation linkage.) The deduced ILTAT 1.3 amino acid sequence is identical to the VSG 117 sequence at this proposed cleavage and glycosylation site; this suggests that both proteins undergo similar processing events. The hydrophobic C-terminal sequence is preceded by a 25–26-amino acid region that is extremely hydrophilic and contains four of the invariant cysteine residues. This hydrophilic region is preceded by a conserved uncharged polar region of 17–18 residues that, in turn, is preceded by another hydrophilic region containing the other four invariant cysteine residues. The amino acid sequences then begin to diverge and very little homology is detected beyond 120 amino acids from the C-termini. Nevertheless, as Fig. 4a shows, ILTAT 1.2 and ILTAT 1.3 are similar in this divergent region in that three more sulphhydryl residues and two additional uncharged polar regions occur in the same relative locations.

Figure 5 compares the deduced amino acid sequences of ILTATs 1.1 and 1.4 and Fig. 4b illustrates their common features. Although clearly similar near the C-termini, these two VSGs are less homologous than the other three. The positions of the four cysteine residues closest to the C-termini are conserved within a very hydrophilic region, similar to the other VSGs. But ILTAT 1.1 has additional cysteines further upstream that are not present in ILTAT 1.4. In addition, these two VSGs do not seem to have within their homology a distinctly conserved uncharged polar region flanked by two hydrophilic regions containing cysteines, as do the others.

ILTAT 1.1 has a very hydrophobic C-terminus as do ILTAT 1.3 and VSG 117. As inferred from other data²⁶ on VSG C-terminal amino acids, the last 17 amino acids are not present in the mature ILTAT 1.1. A comparison of this 17-amino acid hydrophobic 'tail' with the 23-amino acid hydrophobic 'tails' of ILTAT 1.2 and VSG 117 shows two similar features in addition to the hydrophobicity. All three terminate with Leu-Leu-Phe and possess a lysine seven residues removed from the proposed cleavage and glycosylation site. The significance, if any, of these similarities must remain speculative.

In summary, the C-terminal homologies of all five VSGs shown in Figs 3–5 preserve the occurrence of a C-terminal hydrophobic domain and the positions of either four or eight cysteine residues within very hydrophilic regions, suggesting that these regions are required for formation of a general three-dimensional structure. No sequence homologies larger than two amino acids occur within the N-terminal portions of the glycoproteins.

VSG subsets based on C-terminal homology

The above discussion suggests that VSGs can be classified into subsets based on C-terminal homology, much the same as the isotype classification of immunoglobulins (IgM, IgG, etc.) even

though the mechanisms of VSG and immunoglobulin gene expression are different^{15,27,28}. This possibility is substantiated by a recent report²⁶ of the amino acid sequences of tryptic glycopeptides at the C-termini of VSG 117 and four other VSGs. These sequences and the corresponding ILTAT sequences are listed in Fig. 6. Clearly, the nine immunologically distinct VSGs for which C-terminal information is available fall into two groups based on these sequences. Holder and Cross²⁶ obtained sequences of internal glycosylated tryptic fragments and these sequences generally support the same grouping into two subsets. Similarly, genomic DNA hybridization experiments using the Southern procedure also support the conclusion that there are sequence subsets of VSGs^{15,28}. In low-stringency hybridization conditions, C-terminal fragments of VSG cDNA hybridize to many regions in the genomic DNA; under high stringency, or using a cDNA containing N-terminal sequences, only one or a few coding regions are detected.

Finally, the genomic DNA hybridization experiments have indicated that at least two different types of DNA rearrangements occur around most, if not all, VSG coding sequences in the trypanosome genome^{14,18,29} and may be involved in the mechanism of VSG expression. In some cases, an 'expression-linked extra copy' (ELEC) of a VSG gene occurs in cells expressing that gene^{18,29}; in other cases, complex DNA rearrangements beyond the 3' untranslated region of the gene seem to occur, rather than an ELEC^{14,18,29}. These two different types of DNA rearrangement do not correlate with the two different sequence homology subsets. For example, VSG 117, ILTAT 1.2 and ILTAT 1.3 belong to the same VSG sequence subset but an ELEC is associated with VSG 117 expression while 3'-distal rearrangements occur next to the ILTAT 1.2 and 1.3 coding sequences.

VSG		C-terminal sequence	
VSG	117	... WENNA	CKD*
VSG	121	... WGETCKD	*
ILTAT	1.3	... WGETCKD	*
ILTAT	1.2	(unknown)	
VSG	55	... GTAETQ	NTTGS*
VSG	60	... ANT	TTGS*
VSG	221	... TGN	TNTTGS*
ILTAT	1.1	... KDGK	TTNTTGS*
ILTAT	1.4	(unknown)	

Fig. 6 Comparison of the C-terminal amino acid sequences of nine different VSGs (taken from Figs 3 and 5 and ref. 26). The exact C-terminal sequences of ILTATs 1.2 and 1.4 are unknown but they are placed in their respective groups on the basis of sequence homologies further into the protein, as shown in Figs 3 and 5. *, C-termini; ●, glycosylation sites described in ref. 26.

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LETTERS TO NATURE

Is a bi-stable beam responsible for the complex radio structure of 3C133?

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It is generally assumed that the extended lobes of radio emission found in many extragalactic sources are powered by oppositely directed supply beams of relativistic particles emanating from the central galactic nucleus^{1,2}. The complexity and asymmetry of the structure in many sources has, however, led to speculation of a 'flip-flop' beam mechanism^{3,4} where energy is supplied alternately to each radio lobe. Recent high resolution observations of the radio structure of 3C133 reveal a complex structure in which rotation of the source axis may have uncovered evidence for such a bi-stable nature of the energy supply. There are, however, several difficulties in such an interpretation.

The source was observed at 1,666 MHz for 13 h in August 1980, using five telescopes of the multi-telescope radio linked interferometer (MTRLI) at Jodrell Bank⁵. The data have been analysed by CLEAN and closure phase techniques⁶. The results are presented as a contour map in Fig. 1 and the main parameters of the components are summarized in Table 1. A restoring beam of 0.4 arc s, rather than the full resolution of 0.25 arc s, has been used to display the extended regions of low surface brightness.

There are four main regions of radio emission. An unresolved central component (C) is coincident with a 21st magnitude galaxy of redshift 0.28 (ref. 7). There is only a single component (D) to the west, but there are two to the east. One of these (B) is very diffuse, and the other (A) is compact and is connected to the nucleus by a narrow jetlike feature. Emission from the heads of all four components has been detected in observations of lower dynamic range with the Cambridge 5-km telescope at 15.4 GHz (ref. 8).

The lack of reflection symmetry in the structure of 3C133 is difficult to explain in terms of twin supply beams which form outer lobes at 'working surfaces' where the beams impinge on the external medium^{1,2}. Any such explanation assumes that there have been at least two outbursts from the central object. In addition, a contrived situation is required in which motion of the galaxy through the external medium⁹ is coupled with either relativistic doppler effects¹⁰, beam instabilities¹¹ or an aniso-

tropic distribution of electron pitch angles¹² to account for the misalignments and number of observed components.

If the outer components were formed at different times, their morphologies might be used as indicators of their relative ages. On such a basis, the compact component A would be the youngest (and this is supported by the still evident jet), the more extended component D would be of intermediate age, and the diffuse component B, which resembles an outer lobe of well evolved source, would be the oldest. There may thus have been three outbursts of activity in 3C133, and as none of the components has a companion of similar age on the opposite side of the nucleus, these outbursts may have been fundamentally one-sided rather than symmetric in nature.

If this is so, the misalignments of the outer components could be explained by a rotation of the source axis similar to that observed in other sources^{13,14}. The brightness distributions across the heads of the outer components are all markedly asymmetric and have their peaks offset in a manner suggestive of clockwise rotation. This implied sense of rotation is substantiated by the observation that the jet is directed to the northern edge of component A.

While it is possible to envisage a one-sided beam which has swung through an angle $>360^\circ$ and has had long quiescent periods between the outbursts, the overall configuration of the

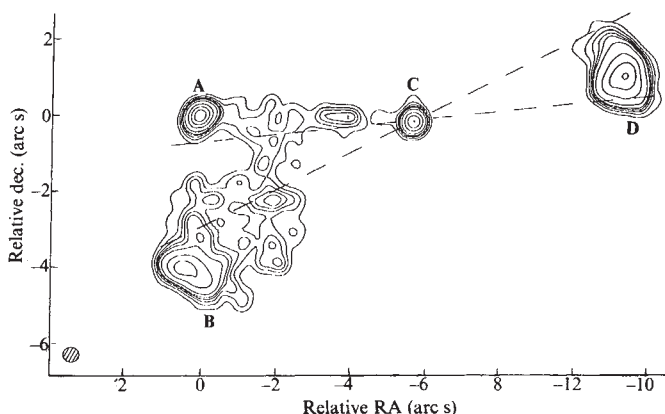


Fig. 1 The MTRLI map of 3C133 at 1,666 MHz. North is to the top and east is to the left. The restoring beam of 0.4 arc s is shown as a shaded circle to the bottom left. The contours are 2, 4, 6, 8, 10, 15, 30, 50, and 75% of the peak brightness of 225 mJy per beam. The broken lines drawn as a guide for the eye are in position angles 94° and 111° .

Table 1 Parameters of components of 3C133

Component	Separation from nucleus (kpc)*	Range of position angles subtended from nucleus (deg)†	Mean component size (kpc)*‡	Flux density at 1.7 GHz (mJy)
C	0	—	<3	205
Jet to component	0–30	86–88	—	45
A	30	85–93	7	450
D	31	94–111(+180)	13	1,020
B	38	114–130	19	(1,510)‡

* Calculated from the source redshift for an Einstein–de Sitter cosmology with $H_0 = 50 \text{ km s}^{-1} \text{ Mpc}^{-1}$.

† Component sizes defined by 20% contours of their peak brightnesses.

‡ The flux density of this component is almost certainly underestimated due to the limited spatial frequency coverage of the observations.

source and the run of position angles subtended by the outer components (Table 1) can be more readily explained by a one-sided beam which has rotated through $\sim 35^\circ$ and has undergone two 180° flips in direction.

The possibility of a bi-stable beam mechanism has been suggested by recent dynamical modelling¹⁵ of an initially spherically symmetric ejection of plasma from the neighbourhood of a supermassive black hole which is embedded in a flattened confining gas cloud. Calculations show that a slight displacement of the black hole from the gas cloud centre will form a one-sided jet along the direction of easiest escape. If the black hole oscillates through or rotates around the gas cloud, there could be a periodic reversal in the direction of the jet.

The observational data allow limits to be set on the time scales of precession and beam reversals for 3C133. From Fig. 1, the position angles of components A and B (measured from C) differ by $\sim 35^\circ$, but any bending of the jet is $\leq 2^\circ$. Therefore, if the rotation of the jet is uniform in the plane of the sky, the rotation period (T_R) must be $> (360^\circ/2^\circ) \times (\text{jet travel time from components C to A})$, that is, $> 2 \times 10^7 \text{ yr}$. The extent of the transverse elongations of components B and D imply that the interval between flips is $\sim 0.05 T_R$, that is, $> 10^6 \text{ yr}$ which is

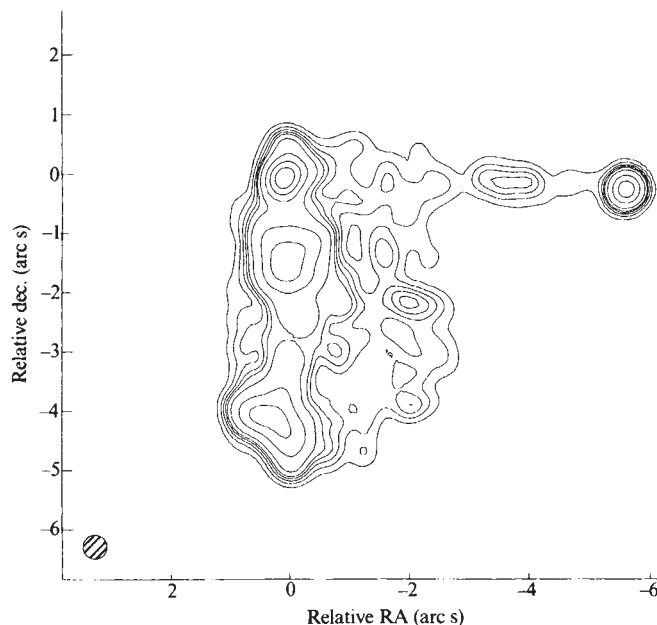


Fig. 2 MTRLI map of 3C133 after the D component has been reflected through the central component. The contours and the restoring beam are the same as for Fig. 1.

consistent with time periods of rotation and z oscillation of galaxies as would be implied by the Wiita and Siah model. In Fig. 2, the major effects of the beam reversals have been artificially removed by reflecting the D component of Fig. 1 through the central component to produce a near-continuous ridge of emission. If the small gaps between the components are due to the evacuation of new channels by the beam, the time scale for the reversal is $\sim 0.02 T_R$ and the component re-evacuation speed is $\leq 0.25c$.

At first sight, the radio structure of 3C133 apparently provides the strongest observational evidence for the existence of a bi-stable or 'flip-flop' beam mechanism. There are, however, two main difficulties with such an hypothesis.

First, if the ordering of relative ages is correct, then the measured flux densities given in Table 1 indicate that the oldest components are the most luminous. If the greater size of the older components is attributable to adiabatic expansion¹⁶, then their past luminosities would have been up to several hundred times greater than at present, implying that the energy supply from the galactic nucleus has decreased dramatically with time over the three outbursts.

Second, the derived beam reversal time scale implies that the age of component B is $> 2 \times 10^6 \text{ yr}$. There is therefore a problem in explaining the detection of emission from all the outer components at 15.4 GHz, as the synchrotron lifetimes of the electrons radiating predominantly at this frequency are $\sim 3 \times 10^5 \text{ yr}$ if the magnetic fields and electrons are in equipartition. This difficulty may be overcome if the rotation is non-uniform, as might be expected if the beams are collimated in the vicinity of a Kerr black hole whose spin axis was initially misaligned with that of the surrounding galaxy¹⁷. If the axes initially differed by $\sim 40^\circ$, but have now swung into near alignment because of the interaction between the angular momenta of the black hole and of the galactic material, then the rotation would originally have been much more rapid, removing the apparent discrepancy between the implied component ages and the synchrotron lifetimes. The similarity of the angles subtended by the components would then imply that the time between beam reversals would have lengthened considerably.

If both the beam luminosity and the length of time that the components are powered have varied, then it seems fortuitous that the outer components all lie at similar distances from the nucleus. Perhaps a simpler solution to the difficulties might be that particle reacceleration occurs in the outer components to produce a delayed brightening of the outer heads after the beam is switched off. It is, however, difficult to envisage such a physical process, and it seems ironic that the need for *in situ* particle acceleration in outer lobes of radio sources was the reason why beams providing a continuous supply of energy were originally postulated.

Despite some problems, a bi-stable beam mechanism seems to offer the most natural explanation for the unusual and complex structure of 3C133. Note, however, that the evidence for such a mechanism is only conspicuous because of the rotation of the source axis. To what extent such switching occurs in normal co-linear sources is unclear, but such a mechanism could explain the complex sub-structure seen in many sources¹⁸, and the one-sided emission of the more compact and possibly younger D2 objects¹⁹.

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Unidentified features in the spectrum of Triton

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Water frost has been identified on the surfaces of the satellites of Jupiter¹, Saturn² and Uranus^{3,4}; methane frost is dominant on Pluto^{5–7}. However, although the IR spectrum of Triton, the largest satellite of Neptune, is similar to that of methane or methane frost⁸, this identification is not consistent with all the available data^{9,10}. We have now used the Multiple Mirror Telescope (MMT) to obtain an improved IR spectrum of Triton. Our observations show features that are not in detailed agreement with the identification of methane, although the general spectral behaviour that led to this identification is confirmed. A satisfactory identification of the surface and/or atmospheric composition on Triton does not yet seem possible.

Observations were made with the circularly variable filter in the MMT IR photometer. The wavelength calibration and spectral resolution of 1% were determined by laboratory measurements of gaseous discharge lamps and were confirmed by measurements of P β and B γ from the planetary nebula NGC7027. All observations were made through a 9 arc s aperture and with reference beam spacing of 20 arc s. Care was taken to ensure that neither the measurement beam nor the reference beams were contaminated by light from Neptune. Observations were carried out on 24.4 April, 13.4 June and 16.4 June 1981 (UT), in all cases very close to maximum elongation of Triton from Neptune. Atmospheric corrections were determined by measuring the solar type star 58 Oph at equal elevation to Triton.

Figure 1a shows the spectrum of Triton, Fig. 1b the same data smoothed to 4% spectral resolution. The error bars are ± 1 s.d. and have been estimated from the reproducibility of repeated spectral scans, on the assumption that the noise level (dominated by detector noise) was the same for all wavelengths. The longest total integration time was devoted to the 1.94–2.12- μ m region of the spectrum; hence, the signal-to-noise ratio is highest there.

The new data are in satisfactory agreement with previous narrow-band photometry of Triton⁹. A previous fully sampled but very noisy spectrum of Triton⁹ agrees in broad outline with the new data but seemed to show high resolution structure that is only partially confirmed by the higher quality data presented here.

The data show the broad absorption near 2.35 μ m which led to the previous identification of methane⁸. There is also a narrower, but resolved, absorption at 2.10 μ m, and possibly an unresolved absorption at 2.00 μ m, an absorption or absorption edge near 1.94 μ m and a broad but shallow absorption at 1.65 μ m. These latter three features are at a 2–3 s.d. level of significance and need to be confirmed at higher signal-to-noise ratio. In addition, the very strong and broad absorption from 3 to 4 μ m (ref. 11) is confirmed by a new measurement with the Infrared Telescope Facility, which shows the average reflectivity between 3.0 and 3.8 μ m to be 0.48 ± 0.05 times the reflectivity at 2.2 μ m. In the visible, the spectrum of Triton is featureless except for a general decrease in reflectivity towards the UV^{10,12}.

The features in the spectrum of Triton could arise directly from the surface material or from gases in a tenuous atmos-

phere, or from some combination. The lower limit of 0.19 for the albedo¹² suggests that the surface may be at least partially frost-covered. Therefore, we have considered the reflectance spectra¹³ of four frosts that are among the most likely candidates for this environment (Fig. 1): H₂O, CH₄, NH₃ and H₂S. These spectra have been smoothed to correspond to a resolution of $\sim 1\%$. None of the frosts provides a satisfactory match to the spectrum of Triton. CH₄ and H₂S frosts are probably also too reflective from 3 to 4 μ m to be consistent with the observations of Triton. We have failed to find a satisfactory match to the spectrum of any other frost.

At the temperature appropriate for the surface of Triton, only a few molecules have sufficiently high vapour pressure to form an atmosphere. Of these, the only two which are likely to be present on the basis of normal solar abundances and which are spectrally active in the 1.6–2.4 μ m region are CH₄ and CO. Either of these gases can account for the broad absorption near 2.35 μ m; however, CH₄ would then produce an absorption of nearly equal strength from 1.65 to 1.8 μ m, and CO would not be absorbing between 3 and 4 μ m.

Recent studies¹⁰ have placed an upper limit of 1×10^{-3} amagat on the atmospheric CH₄ abundance on Triton. The absence of any absorption centred at 1.7 μ m in our spectrum places an independent limit of 1.5×10^{-3} amagat on the atmospheric CH₄ abundance. The absorption feature near 2.35 μ m is two to three times stronger than would correspond to an atmosphere of CH₄ at these limits. It therefore seems unlikely that CH₄ as either gas or solid is the dominant spectrally active constituent on Triton.

A combination of surface and atmospheric absorptions might resolve some of these discrepancies—for example, many hydrated minerals and frosts are very dark between 3 and 4 μ m, so that a CO (and possibly methane) atmosphere over a rocky or frosty surface might fit the data. However, the absorption feature at 2.10 μ m remains an anomaly. Very few of the

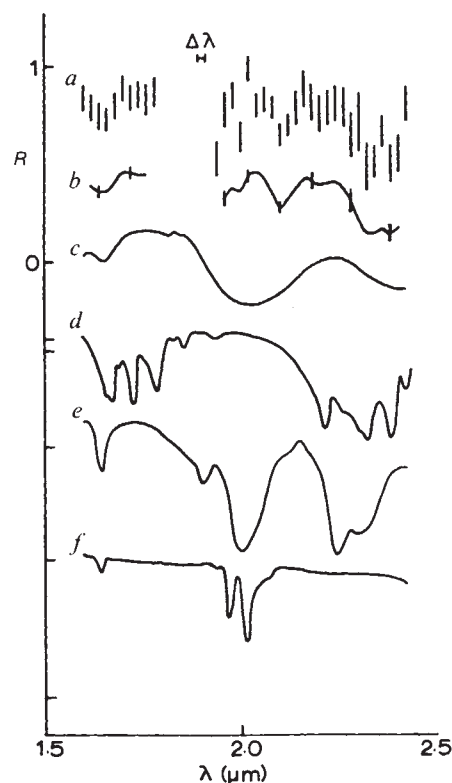


Fig. 1 Reflectivity of Triton and selected frosts. a, Arbitrarily normalized reflectivity of Triton at the original spectral resolution of 1.0%. Error bars are ± 1 s.d. b, Data of a smoothed to 4% resolution. The zero point for this and the subsequent curves are indicated by tick marks on the vertical axis. c, Reflectivity of H₂O frost. d, Reflectivity of CH₄ frost. e, Reflectivity of NH₃ frost. f, Reflectivity of H₂S frost.

molecules likely to be abundant on Triton produce features at this wavelength, and the few which do (such as N_2O) do not match the remainder of the spectrum satisfactorily.

The surface compositions of small bodies in the outer Solar System have generally followed a simple pattern: a single material from a small list of those likely to be abundant dominates their IR reflection spectra. Triton seems to violate this pattern. Further improvements in the observations and in the laboratory spectra of candidate materials will be required to analyse the surface of Triton.

The Multiple Mirror Telescope Observatory used for the present research is a joint facility of the University of Arizona and the Smithsonian Institute. The photometry at $3.5\ \mu\text{m}$ was taken with the Infrared Telescope Facility, which is operated by the University of Hawaii under contract from NASA. Assistance with the observations was provided by B. Kindred and B. Light. We acknowledge helpful discussions with D. Cruikshank, U. Fink and G. Sill. This work was supported by NASA.

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Morphology of iodine-doped polyacetylene

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Although the synthesis of polyacetylene powders was first carried out many years ago, Ito *et al.*¹ have only recently obtained films which can be doped with various chemical species, such as I_2 , SbF_5 or Na, K, giving p or n type semiconductors. These and other properties, such as its optical bandgap² ($E_g \approx 1.5\ \text{eV}$) have made polyacetylene an interesting material for study^{3–6}. Its mechanical stretching ability, for example, leads to partially oriented fibrils and an electrical conductivity anisotropy $\gamma_{\parallel}/\gamma_{\perp} \approx 10$ has been measured⁷ with $\gamma_{\parallel}$ reaching $3 \times 10^3\ \Omega^{-1}\ \text{cm}^{-1}$ when highly doped with AsF_5 ; roughly 12 orders of magnitude higher than the value measured on undoped *cis* (CH)_x. Polyacetylene is available in two isomeric configurations (*cis* and *trans*, Fig. 1). More than 98% *cis* isomer is obtained if the synthesis is performed at low temperatures (-78°C) but it is not thermodynamically stable and becomes *trans* on increasing the temperature, the total transformation occurring when $T > 100^\circ\text{C}$. Any doping process induces a partial *cis/trans* isomerization⁸. The exact conduction mechanism is poorly known: the localization and nature of the doping species have been widely discussed. Here we investigate, using scanning electron microscopy, the behaviour of the morphology of (CH)_x films when the dopant concentration varies. Starting from the fibrillar structure we have observed the formation of aggregates and a uniform melt of various globular features at high doping levels. Our results yield information on how the electrical conductivity takes place in these non-uniform materials.

Acetylene was polymerized, using Shirakawa's technique¹, on the surfaces of a glass reactor. The essential experi-

mental conditions are: solvent, toluene; Al/Ti ratio of 4; catalyst concentration, $0.3\ \text{Ti mol l}^{-1}$; ageing of catalyst, 1 h; temperature, -78°C ; acetylene pressure, 1 atm. The $100\text{-}\mu\text{m}$ thick films obtained were carefully washed in toluene. The *cis*-rich (CH)_x samples were doped with iodine vapour in equilibrium with its liquid phase at 25°C , samples were then pumped for 2 days to remove the interfibrillar non-fixed dopant molecules. The dopant concentrations were evaluated from the weight increase. At low doping levels, the concentration y , defined by $(CHI_y)_x$, is a mean value over the whole sample, taking into account the fact that the macroscopic diffusion coefficient⁹ of iodine in (CH)_x films is $\sim 10^{-8}\ \text{cm}^2\ \text{s}^{-1}$. All our observations were made in the middle of the section of the films to avoid any boundary effect, and the samples were fractured under liquid nitrogen to avoid stresses.

Gold coating was performed by sputtering, the thickness of the obtained film being in the range $50\text{--}100\ \text{\AA}$. Scanning electron micrographs were performed using a JEOL JSM 35 instrument working with an electron beam energy of 20 keV, and a current $< 1\ \text{nA}$ to avoid any radiation damage.

On the first micrograph (Fig. 2a) we observe the fibrillar structure of the undoped *cis*-rich (CH)_x, where a few globular features appear. For $y \approx 10^{-2}$ (Fig. 2b) we note white areas as well as the formation of large aggregates. With $y \approx 0.03$ (Fig. 2c) we observe: (1) an extension of the large aggregates; (2) a regression of the fibrillar structure, which seems to be masked; (3) the appearance of many small white points. We also observe that the true volume occupied by the material is enhanced along Fig. 2a to c. For $y \approx 0.14$ (Fig. 2d), all the platelets and fibrils are recovered with the white points whose size has increased. With $y \approx 0.3$ (Fig. 2e) the observed background is very homogeneous and spattered with large white points.

It has been shown elsewhere that the fibrillar structure is modified when the dopant concentration increases, so we performed another experiment to find out whether the fibrils were masked or destroyed. A (CH)_x film was iodine doped up to $y \approx 0.30$ and then the dopant was extracted by plunging the doped film in toluene with granular silver to form AgI. After a week, the dopant concentration in the film had fallen to $y \approx 0.1$: Fig. 2f shows clearly that the fibrillar structure remains, although their length is reduced and their diameter enhanced; it seems that the $y = 0.1$ dopant concentration only applies inside the fibrils.

Using a CF_3SO_3H dopant we do not observe white points but a considerable increase in size of the fibrils at high dopant levels leading to the formation of islands.

We have investigated⁹ the dopant diffusion mechanism during the doping process of (CH)_x films and shown that the usual diffusion Fick law's cannot explain the measured dopant profiles through the film—an additional process related to a chemical interaction between dopant molecules and (CH)_x fibrils must be involved which must include two kinds of dopant inhomogeneity: (1) A macroscopic inhomogeneous distribution of doping molecules, as presented above, which disappear on highly doped samples. (2) An inhomogeneity inside the fibrils, which persists for a long time, due to the very low diffusion of

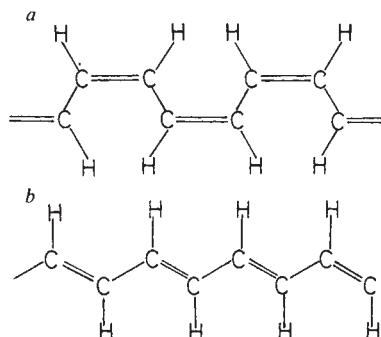


Fig. 1 *Cis* (a) and *trans* (b) isomeric configurations of polyacetylene.

dopant molecules in the crystalline parts of the $(\text{CH})_x$ films, but leads to a rapid production of the observed platelets and to an increase of the diameters of the remaining fibrils.

Finally note that the y values for Fig. 2b–e are an approximate evaluation, the uncertainty is due to the dopant inhomogeneity through the sample discussed above.

Recent experiments¹⁰ and I_2 and SbF_5 doping *trans* $(\text{CH})_x$ seems to produce a more homogeneous doped material but these SEM observations were performed at the film surfaces and not on the cross-section. We have also observed that the surface composition and morphology are uniform at all doping rates⁹, and nearly the same on either side of the film.

To correlate our observations with the electronic transport properties of doped $(\text{CH})_x$, we have plotted on Fig. 3 the electrical conductivity and the corresponding activation energy against the dopant content³ which exhibits a semiconductor to metal transition near 1–3%, depending on the dopant species. At lower dopant levels Rice¹¹ proposed a theoretical model for the electrical conductivity based on the assumption of a very inhomogeneous distribution of the doping species inside the fibrils. In all cases the conducting process was attributed to an extrinsic semiconducting process where an acceptor A^- or a

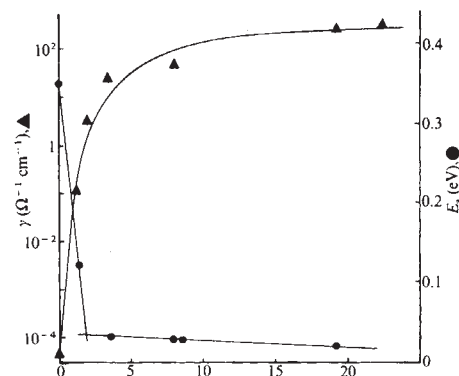


Fig. 3 Typical behaviour of electrical conductivity and deduced activation energy of doped $(\text{CH})_x$ (from ref. 3).

donor A^+ lying near a chain bring, by thermal activation, a carrier which can be delocalized along the chain.

Looking at our present data, taken at various doping levels, some previous assumptions should be revised.

(1) At very low dopant concentrations $y < 10^{-2}$ (Fig. 2b) the presence of fibrils coated with doping species seems likely. However, a chemical reaction between the bulk material and the doping species leads to a rapid production of the observed platelets.

(2) For higher concentrations an important modification of the polyacetylene morphology takes place: fibrils seem modified. In addition, the increasing size and number of white globules with increasing dopant concentration (Fig. 2e) suggest a percolation process to explain the conductivity mechanism (Fig. 3). The slight conductivity increase observed above $y \approx 0.03$ would be due to the variation of the size and conductivity of the elementary clusters. However, these results are obtained when *cis* $(\text{CH})_x$ film is doped at room temperature (25 °C) using the dopant vapour phase in equilibrium with its solid one. We have also verified that similar results are obtained by doping with a pentane solution of iodine if the dopant concentration is high enough.

Consequently we can analyse these observations by way of an inhomogeneous doping process: vapour iodine condense on the fibrils and rapidly react with the polymer to give very highly doped regions. The percolation process could be a consequence of this dopant concentration inhomogeneity in the sample.

These assumptions are also compatible with the effect of dopant concentration on the thermoelectric power and far IR absorption. Note that such a percolation model, implying conductivity between metallic particles embedded in a dielectric continuum, has also been proposed by Mortensen *et al.*¹¹

In conclusion our first experiments, using scanning micrograph analysis, on the doping effect on the polyacetylene morphology indicate that, at very low ($y \leq 10^{-2}$) dopant concentration, the dopant may produce the same effect as that of an impurity on an inorganic classical semiconductor of increasing the carrier number; at higher concentration, that is, around the semiconductor to metal transition region and above, the fibrillar structure seems modified.

Elsewhere the fibrillar structure evolves leading to short fibrils, the diameter of which is largely increased. Consequently the morphology of the doped material strongly depends on the polymerization and doping conditions.

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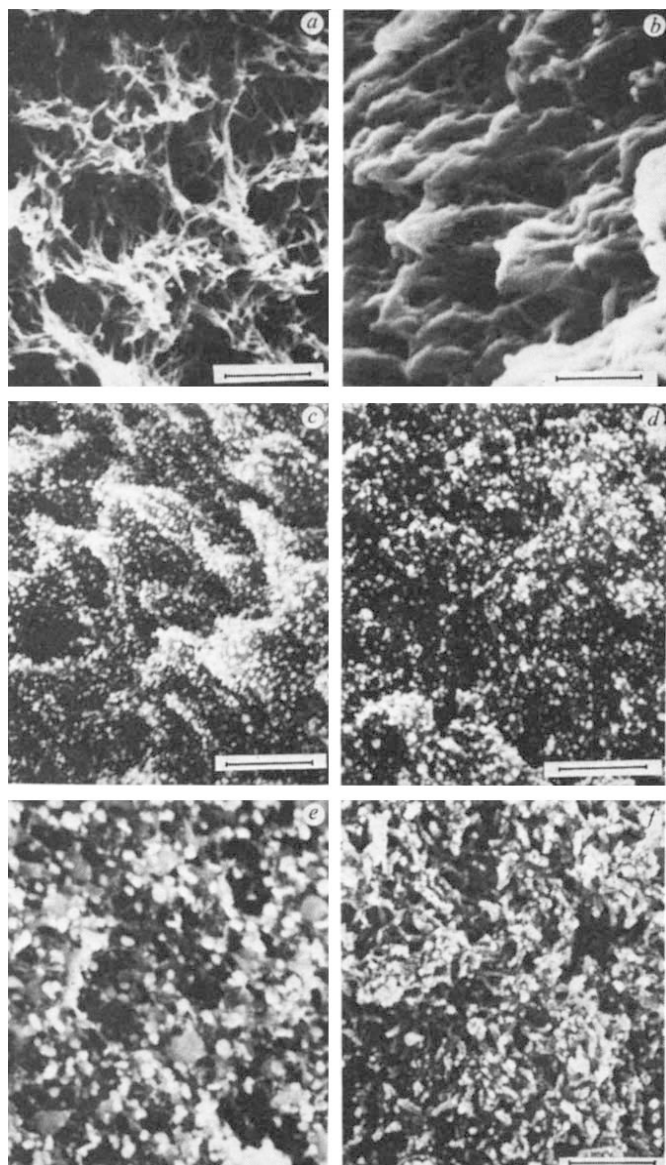


Fig. 2 Scanning electron micrographs of cross-sections of $(\text{CH})_x$ films (150 μm thick) sputter-coated with 80 Å of gold. Scale bar for all micrographs, 1 μm . a, Undoped *cis* $(\text{CH})_x$; b, iodine doped $(\text{CH})_x$ with $y = 0.01$; c, $y = 0.03$; d, $y = 0.1$; e, $y = 0.3$. f, Sample of e after a partial desorption of the dopant, residual $y = 0.1$.

Fusion of pyrope at high pressures and rapid crystal growth from the pyrope melt

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Pyrope $\text{Mg}_3\text{Al}_2\text{Si}_3\text{O}_{12}$ is the magnesium end member of the pyrope garnet series, which is an important constituent of the upper mantle. Melting experiments at high pressure are necessary to clarify the chemical heterogeneity in the deep mantle and the origin of various magmas. Some authors have suggested the possibility of the pressure-induced structural change of silicate melts and discussed its importance on the magma generation and the differentiation in the mantle^{1,2}. We report here melting experiments on pyrope at pressures up to 10 GPa as a first stage in extending the pressure range of model systems for the upper mantle and examining the possibility of the pressure-induced structural change of the melt at high pressure. The correlation between the melting curve and the change of the quenched phases from the melt is the first evidence of a structural change of the pyrope melt at high pressure.

Pure pyrope synthesized at 6 GPa and 1,250 °C was used as the starting material. This powder was directly packed in a graphite capsule which is used as a heater. An MA8-type high-pressure apparatus³ was used. Pressure calibration was

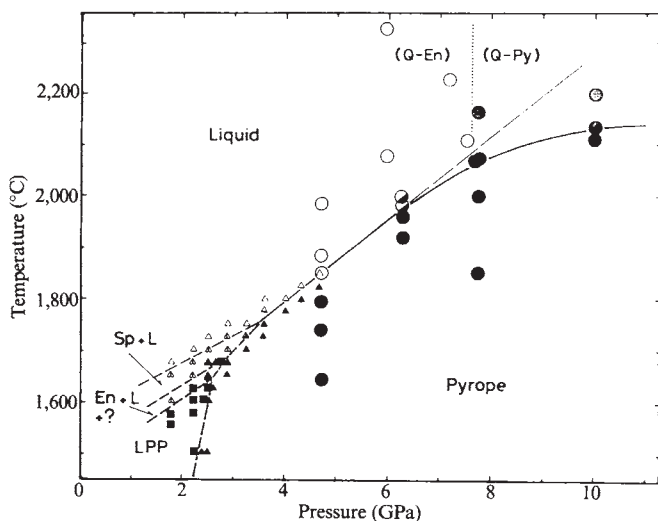


Fig. 1 Melting curve of pyrope up to 10 GPa. The data below 4.7 GPa are from ref. 5 and above this pressure are from the present work. LPP, low pressure phases (mixture of sapphirine, aluminous enstatite, and sillimanite); En+L, aluminous enstatite, undetermined phase (sillimanite or sapphirine?) and liquid; Sp+L, spinel and liquid; ●, pyrope recrystallized without melting; ○, quenched crystal of aluminous enstatite formed from the melt by quenching (Q-En) (glass is also observed below 6.5 GPa); ○●, quenched crystal of pyrope formed from the melt by quenching (Q-Py). The pressure at the change of the quenched phase is shown as a dotted line. The light dashed curve is the extrapolated melting curve fitted to data below 7.0 GPa with the Kraut-Kennedy equation. The curve is expressed as $T(\text{K}) = 1,708(1 + 9.5\Delta V/V)$, where $\Delta V/V$ is calculated using the Birch-Managhan equation of state with the available low-temperature bulk modulus and its pressure derivative⁹. The discrepancy becomes very large above 7.5 GPa.

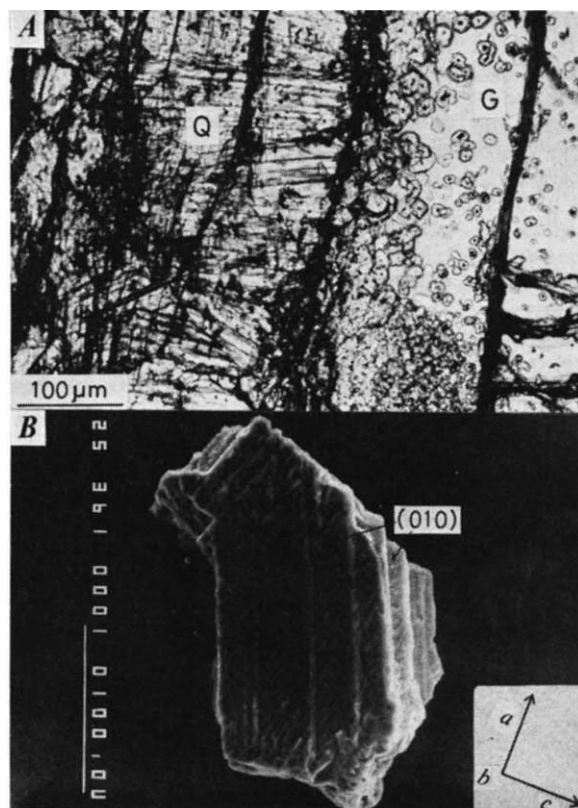


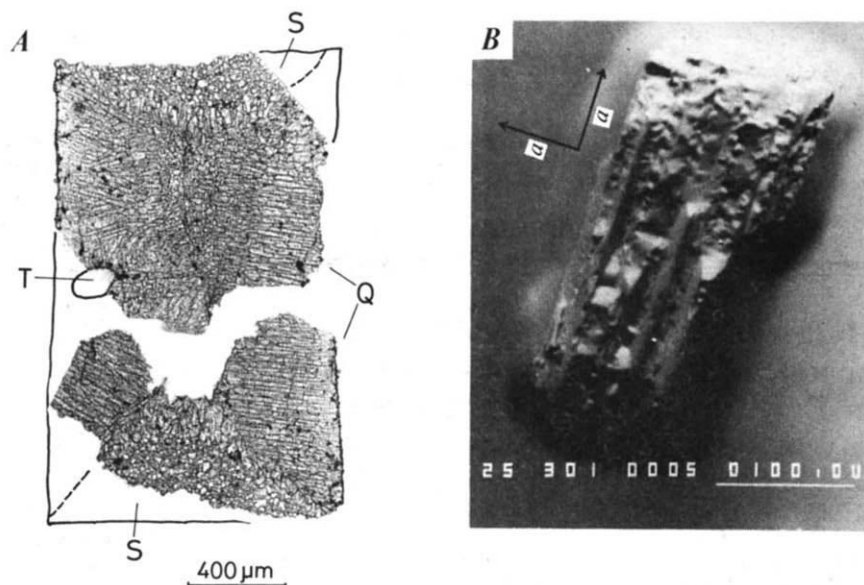
Fig. 2 A, Photomicrograph of the run product quenched from 5 GPa and 1,850 °C. The glassy part (G) and the lamellae of quench aluminous enstatite (Q) are clear. B, Scanning electron image of quench aluminous enstatite. The lamellar texture and the (010) plane are clear. The elongated direction of the lamellae does not coincide with the *c*-axis, and the angle between the elongated direction and the *c*-axis is $69.3 \pm 0.5^\circ$ in this lamellar crystal. The streaks on the (010) plane are also observed in this photograph. Scale bar, 100 μm .

made at high temperature using the phase boundaries of olivine-spinel transition in Fe_2SiO_4 and coesite-stishovite transition determined by a high-pressure X-ray diffraction method⁴. Temperature was measured by a W-W26%Re thermocouple. The quenching method was used to determine the melting curve. The furnace assembly was dried in an oven at about 150 °C for a few hours immediately before each run to avoid the effect of absorbed water on the melting temperature. Pressure was applied to the sample first, and then the temperature was brought to a desired value. Heating was limited to a few minutes to avoid the contamination by the furnace material and the thermocouple to the sample. The sample was quenched isobarically by shutting off the electric power supply. Thin sections of the run products were prepared for microscopic observation and EPMA analysis. X-ray diffraction was also used to identify the run products. Melting was recognized by microscopic observation of the texture of the run products.

Figure 1 shows the melting curve of pyrope up to 10 GPa. The results below 4.7 GPa were obtained by Boyd and England⁵, whereas the data above 4.8 GPa come from the present investigation. As the temperature gradient of the furnace is large; the difference of the temperatures between the central part and the end part of the furnace amounted to $\sim 100^\circ\text{C}$ (ref. 7) only the run products around the thermocouple were selected and examined to determine the melting curve shown in Fig. 1. The present results combined with those of Boyd and England indicate that pyrope melts congruently from 3.6 to 10 GPa. The slope of the melting curve is very large, about 79°GPa^{-1} at pressures below 7 GPa; above this pressure there is a significant decrease. The possibility that the bend of the melting curve originates from an ambiguity of the present pressure scale can be

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Fig. 3 *A*, Photomicrograph of the run product quenched from 10 GPa and 2,200 °C. The quenched pyrope with lamellar texture (Q) is observed clearly. The recrystallized pyrope without melting (S) observed in the end part of the furnace cell is due to the temperature gradient of the furnace. T is the point of the thermocouple. *B*, The backscattered electron image (TOPO) of quenched pyrope. Pyrope quench crystal elongates to [100] direction. Scale bar, 100 μm .



ruled out, because we made the pressure calibration at high temperature using the phase boundaries determined by X-ray diffraction on the basis of NaCl pressure scale⁴ and such bend of the melting curve above 7.0 GPa was not observed in the case of forsterite⁶ and fayalite³ for which the same apparatus and pressure scale were used.

The pyrope melt is quenched to a glass and quench crystal with a lamellar texture below 6.5 GPa. Above this pressure, the run products formed from the melt were aggregates of quench crystal, and the glass was not observed. The quench crystal was aluminous enstatite at pressure below 7.5 GPa. Above 7.5 GPa quench crystals of pyrope were formed in place of aluminous enstatite.

Table 1 X-ray diffraction and chemical data of aluminous enstatite quench crystal

<i>h</i>	<i>k</i>	<i>l</i>	<i>d</i> _{obs} (Å)	<i>d</i> _{cal} (Å)	<i>I</i> _{obs}
0	2	0	4.319	4.322	67
1	2	1	3.266	3.267	17
4	2	0	3.124	3.130	50
2	2	1		3.119	
3	2	1	2.910	2.911	36
6	1	0	2.856	2.856	43
5	1	1	2.811	2.813	21
4	2	1	2.680	2.680	14
1	3	1	2.495	2.495	100
2	0	2		2.494	
5	2	1	2.451	2.450	14
4	3	0	2.431	2.433	7
3	0	2	2.383	2.384	14
3	3	1	2.325	2.326	9
7	1	1	2.241	2.240	10
5	3	1	2.071	2.070	10
5	1	2	2.050	2.050	10
7	2	1	2.045	2.044	9
1	4	1	1.9843	1.9831	14
4	4	0	1.9506	1.9512	14
2	4	1		1.9485	
6	3	1	1.9359	1.9359	10
10	1	0	1.7757	1.7765	9
2	5	0	1.6985	1.6984	10
6	5	0	1.5019	1.5011	11
1	3	3	1.4777	1.4778	17
10	3	1	1.4727	1.4727	17
0	6	0	1.4402	1.4408	86

Cell constants: *a*, 18.152 ± 0.006 Å; *b*, 8.645 ± 0.002 Å; *c*, 5.188 ± 0.002 Å; *V*, 814.06 ± 0.48 Å³. Space group, Pbc_a. SiO₂, 45.13 wt%; Al₂O₃, 24.83 wt%; MgO, 29.80 wt%; total, 99.76 wt%. Numbers of ions on the basis of six oxygens:

Si	1.517	2.000	Al	0.501	1.992
Al	0.483		Mg	1.492	

Figure 2A shows the coexistence of glass and quench crystals formed by quenching from 1,850 °C at 5 GPa. Both the glass and the quench crystal were analysed by EPMA and found to have a pyrope composition. There is no difference in the chemistry of the quench crystal and the glass. The X-ray diffraction pattern of the quench crystal can be indexed as an orthorhombic pyroxene with a space group Pbc_a. According to the EPMA and X-ray diffraction analysis (Table 1), the quench crystal is an aluminous enstatite with a pyrope composition. To our knowledge, this is the first report of a pyroxene with pyrope stoichiometry. The scanning electron image (SEI) of the quenched aluminous enstatite is shown in Fig. 2B where the lamellar texture and (010) plane are clear. The elongated direction of lamellae does not coincide with that of tetrahedral chains along the *c*-axis of the pyroxene structure, and the angle between the elongated direction and the *c*-axis varies from 60° to 70° among the different sheaves of lamellae.

The quenched pyrope formed at pressures above 7.5 GPa has a lamellar texture and can be distinguished from the pyrope crystal recrystallized without melting, which is granular in texture. Figure 3A shows the coexistence of a quenched pyrope and a recrystallized pyrope. The coexistence of these two phases is one of disequilibrium and is caused by the temperature gradient in the furnace. The difference in the textures is clear. X-ray precession photographs indicate that the lamellae elongate parallel to [100] direction and the planes parallel to [100], which are assigned to {011} planes, are also observed. The backscattered electron (TOPO) image of the quenched pyrope is shown in Fig. 3B. The quench crystal from the pyrope melt changes from aluminous enstatite to pyrope around 7.5 GPa in accordance with the bend of the melting curve.

The bend of the melting curve can be explained by a volume decrease of the melt due to a pressure-induced structural change. The structural change of the melt by a shifting of Al ions from fourfold to sixfold coordination has been suggested by Waff². Recent Raman spectrometry of the jadeite glass synthesized at pressures up to 4 GPa indicated that there was no evidence of a coordination change of Al ions⁷. However, this type of the structural change in the melt can be expected to occur at even higher pressure. Al ions occupy both tetrahedral and octahedral sites in aluminous enstatite, while all Al ions occupy the octahedral sites in pyrope. As has been reported, some pyroxenes transform to the garnet structure at high pressure⁸. Then the change of the quench crystal from pyroxene to garnet in accordance with the bend of the melting curve may suggest such a pressure-induced coordination change of ions in the pyrope melt at high pressure.

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Hydrazines and carbohydrazides produced from oxidized carbon in Earth's primitive environment

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Our ideas of the possible composition of the atmosphere of the primitive Earth have broadened markedly since Oparin's¹ and Urey's² postulates of a highly reducing atmosphere containing hydrogen, ammonia, hydrocarbons and water. Since then, various geochemical models of the primordial atmosphere have been proposed³⁻⁶. Of importance is whether abiological organic compounds can be formed from the interactions of energy sources with nitrogen, oxidized carbon and water. Experiments involving electrical discharge^{5,7} and bombardment with beams of He ions⁶ of various mixtures of CO, CO₂, N₂, H₂ and H₂O suggested that formic acid was the major organic product. We now report experiments using quenched spark discharges through molecular nitrogen on aqueous suspensions of CaCO₃, and other reactants to simulate the atmosphere/hydrosphere interface. Hydrazine and carbonylhydrazide are recovered in significant but low yields. Their reactions in primitive aquatic environments could have supplied a pathway for chemical evolution and the origin of life on a primitive Earth in which carbon in the fully oxidized states was available for the primary synthesis of organic matter.

Our experiments were designed (1) to supply aqueous inorganic carbon in the form of calcium carbonate to effect pH control near pH 7.5–8.0 as well as to provide dissolved CO₂ and dissolved CO₃²⁻ anion in constant small amounts determined by the low solubility product of CaCO₃, and (2) to supply Fe⁰ to act as a scavenger for oxidizing agents. We believe that such a system corresponding to a primordial atmosphere/hydrosphere interface is suitable for assessing potential pathways for organic synthesis where carbon is in the +4 oxidation state.

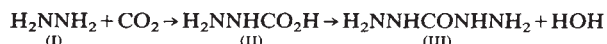
Five-litre flasks equipped with a central nichrome or gold wire electrode and a high-vacuum valve were filled with 50 ml doubly distilled water, 100 mg (1.78 mmol) 400-mesh reduced iron and 100 mg (1 mmol) CaCO_3 . The gas phase was evacuated, purged with nitrogen and filled with 750 mm nitrogen (223.2 mmol). For some experiments, 0.5 mCi NaH^{14}CO (specific activity 50 Ci mol $^{-1}$) was added using a gas-tight syringe through an attached septum. An Electro-Technics high-frequency generator was connected to the central electrode and discharged on the water surface through a capacitatively coupled external metal ground plate. After 10–18 h, the cloudy white suspension of CaCO_3 became clear and the pH dropped from 8.1 to 7.0. At this time, gas chromatographic analysis of the headspace (5 ml samples at ~750 mm) showed no detectable H_2 or O_2 , traces of CO_2 and minute amounts of CH_4 in an excess of unreacted nitrogen.

Chemical analysis of both the water and particulate phases

was negative for nitriles (by pyrohydrolysis and benzidine acetate-copper(II) acetate staining) and for amino acids (by ninhydrin staining). Nitriles present in nanomolar amounts could have been detected by this method. TLC on silica gel plates revealed a single dominant organic component which was detected by iodine vapour, or by rhodamine-B staining, or as a dark spot on silica gel layers containing a 254-nm UV fluorescent dye. The product had the same R_f values as a standard carbonylhydrazide in four solvent systems: (1) butanol/formic acid/water, 17:1:2; (2) CHCl_3 /methanol/8.4 M NH_4OH , 2:2:1; (3) CHCl_3 /methanol/12 M NH_4OH , 85:15:1; and (4) CHCl_3 /methanol/8.4 M NH_4OH , 1:4:1. Standard carbonylhydrazide and a related standard, semicarbazide, were obtained from the Aldrich Chemical Co.

When 0.5 mCi $\text{NaH}^{14}\text{CO}_3$ was included in several such quenched spark-discharge reaction mixtures, 30% of the organic ^{14}C -labelled products migrated with R_f values identical to carbonylhydrazide in the above TLC solvent systems, while the balance remained at the origins. (The organic carbon products remaining at the origins have not been firmly identified, although when subjected to 6 M HCl hydrolysis at 120 °C, ninhydrin-positive and UV chromatophores were released.) In one typical experiment, 1,200 d.p.m. total organic carbon per 40- μl sample (1.5×10^6 d.p.m. per 50.5 ml total reaction volume) were recovered after addition of 6 M HCl at 25 °C to decompose unreacted carbonate. Of this total, 0.42×10^6 d.p.m. (28%) behaved identically to carbonylhydrazide on the chromatograph. If we assume both labelled NaHCO_3 and unlabelled CaCO_3 to be equally reactive, the carbonylhydrazide yield was 0.38 μmol , and the total organic carbon yield 1.38 μmol . This latter value indicates conversion of 0.14% of the initial carbonate to organic carbon.

Carbohydrazides are used as intermediates in various organic synthetic reactions^{8,10,11} and undergo many reactions similar to hydrazine. Hydrazine is implicated as an intermediate in the reactions leading to carbohydrazide formation, because carbohydrazide (III) is a major carbon-containing product and its synthesis results from reactions of hydrazine (I) with carbon dioxide via carbazic acid (II) as an intermediate^{9,10}:



Tests for hydrazine in the water phase of these reactions were positive, as determined by TLC of its yellow *p*-dimethylamino benzaldehyde azine derivative and quantitatively using the ASTM standard test D-1385-18 for hydrazine in water, and confirmed by combined gas chromatographic/mass spectrometric analysis. Table 1 presents the data for the synthesis of hydrazine in various reaction conditions. Assuming linearity, the maximal rate of synthesis was $0.83 \mu\text{mol hydrazine h}^{-1}$; the rate decreases after ~ 10 h, coincidentally with the apparent loss of solid CaCO_3 .

Table 1 also summarizes data on the presence of carbohydrazide, the final pH and other observations for various combinations of reactants in quenched spark discharge experiments. Note that hydrazine is always present with carbohydrazide. Carbonate is required and the pH must be maintained near or above 7.0 during most of the hydrazine/carbohydrazide synthesis. Reduced iron is not required to scavenge oxidants, but dinitrogen appears to fulfil this role, as manifest by the relatively large amounts of nitrite and nitrate seen in all experiments. The data so far do not indicate whether solid carbonate or soluble carbonate anions are involved when CaCO_3 is used. If carbon is present as CO_2 , no hydrazine nor carbohydrazide is formed. Neither Ca^{2+} nor Na^+ anions will lead to the synthesis of hydrazine or carbohydrazide in the absence of carbonate. When air was substituted for nitrogen, hydrazine and carbohydrazide yields were similar to the anoxic experiments. In all cases, carbohydrazide is only found when hydrazine is synthesized, supporting our suggestion that its synthesis proceeds via carbazic acid, as proposed by others^{9,10}:

These experiments show that, in anoxic prebiotic or contemporary atmospheric conditions, in the absence of molecular

Table 1 Products obtained by quenched spark discharge on various reactants

Reactants	Products (yields are total material recovered per flask after 10 h sparking)	(Initial final pH)
A		
750 mm N ₂ ; 1 mmol CaCO ₃ ; 1.78 mmol Fe; 50 ml H ₂ O	5.86 µmol hydrazine; 0.5 µmol carbohydrazide; 870 µmol NO ₂ ; 1,130 µmol NO ₃	(8.1) 7.3
750 mm N ₂ ; 1 mmol CaCO ₃ ; 50 ml H ₂ O	8.28 µmol hydrazine; 0.5 µmol carbohydrazide; 316 µmol NO ₂ ; 74 µmol NO ₃	(8.1) 6.6
750 mm N ₂ ; 1 mmol NaCO ₃ ; 1.78 mmol Fe; 50 ml H ₂ O	6.84 µmol hydrazine; 0.5 µmol carbohydrazide; 265 µmol NO ₂ ; 1,675 µmol NO ₃	(8.2) 3.5
750 mm air; 1 mmol CaCO ₃ ; 50 ml H ₂ O	5.07 µmol hydrazine; 0.5 µmol carbohydrazide; 640 µmol NO ₂ ; 1,080 µmol NO ₃	(8.1) 7.1
B		
750 mm N ₂ ; 1.78 mmol Fe; 50 ml H ₂ O	<0.02 µmol hydrazine; carbohydrazide, not detected; >500 µmol NO ₂ ; >1,000 µmol NO ₃	(6.0) 4.2
750 mm N ₂ ; 30 mm CO ₂ ; 50 ml H ₂ O	<0.01 µmol hydrazine; carbohydrazide, not detected; >500 µmol NO ₂ ; >1,000 µmol NO ₃	(5.2) 1.1
750 mm N ₂ ; 20 mm CO ₂ ; 1.78 mmol Fe	<0.01 µmol hydrazine; carbohydrazide, not detected; >500 µmol NO ₂ ; >1,000 µmol NO ₃	(5.0) 1.1
750 mm N ₂ ; 1 mmol CaCl ₂ ; 50 ml H ₂ O	<0.01 µmol hydrazine; carbohydrazide, not detected; NO ₂ /NO ₃ not measured	(5.0) 1.4
750 mm N ₂ ; 1 mmol NaCl; 50 ml H ₂ O	<0.01 µmol hydrazine; carbohydrazide, not detected; NO ₂ /NO ₃ not measured	(5.0) 1.4
Control		
750 mm N ₂ ; 1 mmol CaCO ₃ ; 50 ml H ₂ O; No spark	<0.01 µmol hydrazine; carbohydrazide, not detected; NO ₂ /NO ₃ not detected	(8.0)

A; those reaction conditions which lead to the synthesis of hydrazine and carbohydrazide. B, those reaction conditions which lead to the oxidation of molecular nitrogen. Nitrate and nitrite were measured according to ref. 15.

hydrogen: (1) molecular nitrogen can be reduced to hydrazine; (2) oxidized carbon is reduced to organic carbon products of which one-third is carbohydrazide; (3) molecular nitrogen serves as the primary oxidant scavenger, leading to the formation of nitrite and nitrate.

The significance of these simulated processes in the routes to organic matter from oxidized carbon in a mildly reducing prebiotic Earth model remains to be assessed. Nonetheless, the yields reported here, though lower than in similar systems containing methane¹³, are much higher than achieved earlier in systems containing fully oxidized carbon^{5,7}. This suggests that organic synthesis in prebiotic surface environments consonant with previous models³⁻⁶ merits further investigation. More productive processes may yet be found; further studies of similar heterogenous systems are underway.

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Temperature and precipitation record in southern Chile extended to ~43,000 yr ago

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Southern Chile (41–56°S), in the belt of westerly winds, receives mostly heavy precipitation, reaching 8,500 mm yr⁻¹ near 50°S and decreasing northwards and southwards from this latitude to ≤1,500 mm; mean January (summer) temperatures near sea level along the latitudinal gradient are 8–16 °C (refs 1, 2). Dense rain forest covers much of the region to 48°S; south to Cape Horn, magellanic moorland prevails and rain forest becomes limited. Modern pollen measured in surface samples reflects the distribution of plant species in the vegetation. We have now applied regression equations relating present-day pollen to temperature and precipitation to fossil pollen data at Taiquemó to assess climatic conditions during the Quaternary. The results extend our previous record of the past 16,000 yr at Alerce³ beyond the lateglacial to ~43,000 yr BP. For the 27,000-yr interval, they show mean January temperatures of 10–12 °C and mean annual precipitation centred around 1,000 mm except during the time span of ~31,000–43,000 yr BP when amounts increased to 4,000 mm. In general fluctuations correspond to the isotopic climatic reconstruction in Antarctica⁴ and to changes inferred from pollen data at comparable latitudes in Tasmania⁵⁻⁸ and New Zealand^{9,10}.

We derived temperature and precipitation data from the pollen contained in sediments in a lake basin at Taiquemó (42°10'30" S, 73°35'45" W)¹¹. The site is located on northeastern Isla Chiloé at an elevation of 170 m, 105 km south-west of Alerce where we reported quantification of southern Chile climatic change to 16,000 yr ago³. The basin is situated at the outer edge of an end moraine that is partially cutover and occupied by remnants of Valdivian rain forest. The moraine seems to date from the middle part of the Llanquihue (Wisconsin) Glaciation, the last glacial age to affect Isla Chiloé. A 760-cm core from the basin is ¹⁴C dated to 42,700 ± 1,200 (QL-1011) and to 42,400 ± 1,000 (QL-1012) yr BP at the respective 700-cm and 760-cm levels; these and six additional ages establish the chronology of the core sediments.

Data for the sediments in the core (Table 1) show peat beds in the upper 200 cm and below 560 cm interbedded by gyttja. The upper bed began forming at 14,120 yr BP and the lower bed formed from ~43,000 until before 31,200 yr BP. Loss on ignition measurements indicate that percentages of organic matter in the core are lowest during the lacustrine phase between 200 and 560 cm; the sedimentation rate over the 43,000-yr interval was lowest during the latter part of this phase from 20,100 to

Table 1 Sedimentary data for the Taiquemó core

Depth (cm)	Sedimentary material	% Average weight loss on ignition	Age interval (^{14}C yr)	Sedimentation (yr cm^{-1})	Average pollen density (grains cm^{-3})	Average pollen influx ($\text{grains cm}^{-2} \text{yr}^{-1}$)
0–160	Peat	80	0–12,000	75	36×10^3	500
160–200	Peat	84	12,000–14,120	53	87×10^3	1,600
200–260	Gyttja	27	14,120–20,100	100	39×10^3	400
260–300	Gyttja	9	20,100–21,900	45	20×10^3	400
300–400	Gyttja	14	21,900–26,600	47	22×10^3	500
400–490	Gyttja	18	26,600–31,200	51	59×10^3	1,200
490–700	Gyttja-peat	31	31,200–42,700	55	211×10^3	3,800
700–760	Peat-sand	63	42,700–42,400	55*	423×10^3	7,700

*For this interval, the same rate as between 490 and 700 cm is assumed.

14,120 yr BP. Pollen influx is relatively low; averages are higher for the peat than for the gyttja, with highest values in the basal peat.

The temperature and precipitation equations were produced by stepwise regression, using normalized per cent averages of 20 pollen taxa as predictors. Although the taxa are moderately intercorrelated (maximum $r = 0.69$), orthogonalization of the variables failed, even after rotation, to produce a biologically convincing solution. A total of 59 composite sites (160 surface samples) was used for estimating temperature and 57 for precipitation. Addition of 33 composite sites from the rain forest of Tierra del Fuego¹² enlarged the data set on which Alerce estimates were based. Application of the new equations to the Alerce data gave results in agreement with trends reported previously. The new equations seem, however, to be much more sensitive to observed variations in the older pollen record at Taiquemó. The temperature equation has seven terms that explain 82% of the variance; the standard error of estimate is 0.96°C (12% of the range of surface temperatures). The precipitation equation has nine terms accounting for 86% of the variance; the standard error is 415 mm (11% of the range of surface values). Plots of observed versus predicted temperature and precipitation indicate that the equations are reasonably structured within the limitations of the surface data set. Pollen spectra occasionally occur which seem to correspond with vegetation from warmer and wetter sites outside our surface data range. The equations predict excessively warm and wet conditions at these levels. Expansion of the surface data base would probably remedy this but samples are not available. Similarly, there seems to be some distortion of the record at the lower temperatures. Despite these limitations, we believe that trends are correctly described.

When applied to the fossil pollen stratigraphy at Taiquemó, the equations produce curves (Fig. 1) that can be fitted to the trends of temperature and precipitation between ~12,000 and 16,000 yr BP at Alerce. Only this portion of overlap in the two sets of data is shown to simplify the fit; the younger portions of the Taiquemó curves, represented by only 16 stratigraphical levels, lack a chronology and the detail shown by the 73 levels at Alerce. Accordingly, we have omitted data younger than 12,000 yr BP at Taiquemó in favour of the entire Alerce record.

Results indicate a mean January temperature of $\sim 10^\circ\text{C}$ between 14,120 and 31,200 yr BP. This followed a decrease from 12°C around 43,000 yr ago. Minimum temperatures over the time span are $\sim 4^\circ\text{C}$ lower than present-day ones at Taiquemó. Precipitation is $< 1,000$ mm from ~14,000 until 21,900–26,600 yr BP; values are greatest before 31,200 and register a distinct rise to $> 4,000$ mm around 43,000 yr BP. The range over which precipitation changes is $> 3,000$ mm and is $> 1,500$ above and below the modern mean of 2,600 mm. The long intervals with limited frequency variations shown in the pollen profiles at Taiquemó¹¹.

Interstadial conditions at Taiquemó were clearly wetter and warmer around 43,000 yr BP. Precipitation has fluctuated less

but noticeably since then until ~14,000 yr BP, while changes in temperature are only $\leq 1^\circ\text{C}$. The minor increase in precipitation with no perceptible increase in temperature between 26,600 and 31,200 yr BP represents an apparent climatic event. The interval is also recognized in the pollen stratigraphy at Río Teguaco, 13.5 km directly south of Taiquemó, where it is ^{14}C dated to between $25,500 \pm 500$ (QL-1017) and $30,000 \pm 300$ (QL-1019) yr BP. Drier and colder climate existed at Taiquemó during a stade that lasted until at least 14,000 yr ago. These climatic changes seem consistent with what is broadly known of glacier fluctuations in the region during the Llanquihue Glaciation^{11,13,14}.

Overall relationships can be drawn between the behaviour of the curves at Taiquemó and climatic conditions recognized from other data sources in the middle and higher latitudes of the Southern Hemisphere. The estimated 32,000-yr oxygen isotope

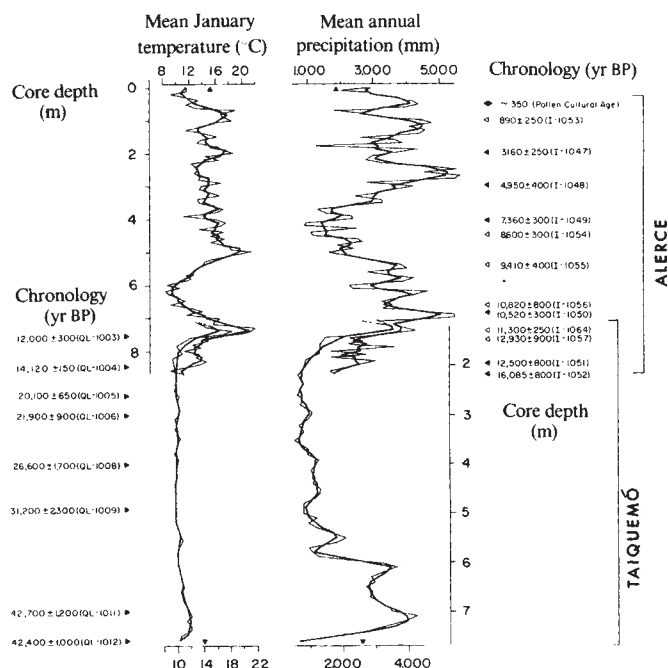


Fig. 1 Mean January temperature and mean annual precipitation at Alerce (upper scales) and Taiquemó (lower scales) for the past ~43,000 yr. Bold lines represent three-point moving averages of the data. Triangles on the temperature and precipitation scales indicate the modern means; ^{14}C ages are also indicated by triangles (closed ones relate to the cores whereas open ones for Alerce and Taiquemó scales are offset slightly to align the curves).

stratigraphy for the Dome C ice core from east Antarctica⁴ indicates trends that are approximately parallel despite the degree of uncertainty in the Dome C chronology, which is taken from ¹⁴C ages of a marine core in the Indian Ocean. Major isotopic shifts indicate slightly ameliorated conditions before 25,000 yr BP, cold with decreased snow accumulation until ~16,000 yr BP (the time of the maximum advance of the West Antarctic Ice Sheet between 21,200 and 17,000 ¹⁴C yr BP)¹⁵ and finally a warming trend that became stabilized close to 10,000 yr BP with minimal changes thereafter. Because of the uncertainty of the Dome C chronology, it is not possible to interpret certain changes in the stratigraphical record. This difficulty also applies to comparison of marine data with the Chilean data; however, estimated sea surface temperature profiles, derived from radiolarian assemblages in conjunction with oxygen isotope stratigraphy in marine sediments of the subAntarctic, do show the same trends as those at Taiquemó over what is interpreted to be the same time interval¹⁶.

Pollen data from Tasmania⁵⁻⁸ and New Zealand^{9,10} in the zone of westerly winds (41–43 °S) are probably more relevant to the Taiquemó sequence of interstadial and stadial climates. At Blakes Opening in south-central Tasmania, a wetter and to some extent warmer interstade, when temperate rain forest developed, is ¹⁴C dated earlier than 41,150 ^{+1,450}/_{-1,250} until ~53,400 yr BP; later, wet sclerophyll forest succeeded in cooler and less humid conditions. The same climatic changes are apparent at Pulbeena and Mowbray Swamps in north-west Tasmania where grassy eucalyptus woodland or scrub in a cool, moist climate before 35,000 yr BP was followed by grassland associated with cold and lower humidity through the lateglacial. In northwestern South Island, New Zealand, the cold, relatively dry climate indicated by grassland continued until ~12,000 yr ago, except for an interstade characterized by shrubland with some spread of southern beech from ~26,000 until before 31,000 yr BP. Within the time limits set by the ¹⁴C chronology, these successive climatic events correspond remarkably with those apparent from the Chilean record over the same millennia.

We conclude that the trends of temperature and precipitation since ~43,000 yr BP, derived from the application of multivariate statistics to the pollen data at Taiquemó and Alerce, are generally representative of the Quaternary climates thus far established from some middle-latitude sites in the Southern Hemisphere. It should be possible to quantify further temperature and precipitation to demonstrate the degree of correspondence between land mass records through the last interglaciation. Fossil pollen records in this time range are available^{8,17} but require quantification of the climatic variables from the pollen data.

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Palaeomagnetic excursions, aborted reversals and transitional fields

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Recordings of palaeomagnetic excursions have revealed apparent field behaviour ranging from rather erratic directional movements and loopings¹⁻⁴ to single, highly defined events⁵⁻⁷. Excursions of the latter variety show what seems to be a rapid change in direction such that the path of the associated virtual geomagnetic poles (VGPs) is well constrained in longitude. Such behaviour is not unlike that observed at the onset of some recorded polarity transitions⁷⁻⁹. Indeed, it has been suggested that excursions may occur during unsuccessful, or aborted, reversals^{2,5-7,10}. We show here that available records of palaeomagnetic excursions, together with our present understanding of field behaviour associated with geomagnetic reversals, strongly support this hypothesis.

The ultimate question is: is it reasonable to consider at least some identifiable palaeomagnetic excursions to be records of aborted reversals and, therefore, relevant to our investigations of transitional field behaviour? If so, such data would provide a second major source of palaeomagnetic information to further our understanding of transitional field configurations and geomagnetic reversal.

It is first necessary to identify those palaeomagnetic recordings of claimed excursions which are the most likely to display accurately geomagnetic behaviour. As it is very important that the derived set of acceptable excursion records is not contaminated by spurious, inaccurate, or deceptive data, cautious and stringent criteria for acceptability must be imposed. For example, palaeomagnetic excursion data obtained from sediments will not be considered here, although they may include one or more reliable recordings (for example, ref. 4) because of the controversies and uncertainties surrounding many sediment-recorded excursions^{3,11}. Similarly, excursion data obtained from sites at high latitude will not be considered. Exclusion of Icelandic data is particularly justified, given the relatively close proximity of the recording site to the geographical pole. The effects of secular variation at such high latitudes are known to be more pronounced and, hence tend to conceal systematic field behaviour related to excursion events. This may be the case with regard to Icelandic transition data¹².

Given the above arguments, to be considered acceptable a palaeomagnetic excursion record must: (1) be obtained from igneous rocks; (2) seem to be reliably determined, given the techniques used and results obtained; (3) contain a minimum of three successive data points (such as lava flows) associated with low-latitude (<45°) VGPs; (4) show that the intermediate directions were recorded during a clearly defined polarity state; and (5) be associated with a low or mid-latitude site.

Four excursion records satisfy the above criteria and, each is associated with a sequence of basalt lavas ranging from mid-Tertiary to Pleistocene. Table 1 lists the site description, age and relevant palaeomagnetic data for each. Note that all four of these acceptable excursion records show some longitudinal confinement of the low-latitude VGPs. As mentioned elsewhere, such behaviour is a common characteristic of palaeomagnetic recordings of Cenozoic polarity transitions⁷⁻⁹.

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Table 1 Excursion data

Site location (ref.)	Coordinates	Full polarity sense	No. of low latitude VGPs	VGP path location relative to site*	Meridional band width†	Age	Symbol
Oahu, Hawaii (5, 18)	21.5°N 201.8°E	Reverse	3	+1.7 (Near)	12.6	~3 Myr	●
Amsterdam Island (6)	37.8°S 77.5°E	Normal	5‡	-150.7 (Far)	16.5	Brunhes	▼
Nandewar Volcano, Australia (19)	30.3°S 150.2°E	Normal	5§	+161.9 (Far)	22.4	17.5 ± 0.3 Myr	▲
Liverpool Volcano, Australia	31.7°S 150.2°E	Reverse	3§	-3.6 (Near)	68.8	33.7 ± 0.7 Myr	■

* Mean angular longitudinal distance in degrees of low-latitude VGPs from site meridian (+) east of site, (-) west of site.

† Width of meridional band containing all low-latitude VGPs.

‡ Three of which are successive flows.

§ VGPs calculated with respect to a location for Australia appropriate to the age of the sequence.

|| To be published elsewhere.

However, before comparing further these excursion data with those associated with successful field reversals, I shall briefly summarize our present knowledge regarding directional behaviour during field reversals.

Recently much has been learned about the morphology of transition fields⁹. For example, comparison of palaeomagnetic records of the last reversal has shown the intermediate field to be predominantly non-dipolar^{7,13,14}. Moreover, VGP paths corresponding to this, as well as most other recorded Cenozoic polarity transitions, show a spatial dependence on the locality of the recording site¹⁵. In particular, intermediate VGPs associated with reverse-to-normal (R→N) transitions from sites in the Northern Hemisphere are found almost exclusively on the hemisphere centred about the respective site longitude^{12,15}, the so-called near side. Thus the non-dipolar component(s) controlling transition fields are axisymmetric and of low order^{12,15}. However, our knowledge concerning this site dependence is incomplete. A more thorough understanding of transitional field geometries, as well as recognition of particular systematics associated with reversal in the core, require N→R records from the Northern Hemisphere as well as records of both transition senses from the Southern Hemisphere¹². At present the latter hardly exist⁹.

Two of the four acceptable excursion records correspond to events during normal polarity of the field and three of the recordings were obtained from sites at mid-southern latitudes. Hence, provided they are indeed representative of field behaviour during initiation of a reversal, these excursion records will greatly improve the existing polarity transition data set. Furthermore, provided the corresponding VGP behaviour is unambiguous, the combined successful/aborted reversal data may be sufficient to distinguish the predominant axisymmetric field geometry during transitions. Figure 1 shows the VGP data relative to site longitude, while taking into account the full polarity state of the field at the time of occurrence as well as the hemisphere of the recording site.

Note that the single record obtained from northern latitudes is associated with reverse polarity. Hence, this record serves to test further whether such field behaviour is the result of an unsuccessful reversal attempt. Comparison of the corresponding VGP path (Fig. 1, upper right) with existing R→N transition data⁹ strongly points to the affirmative. Indeed, this excursion path from Oahu, Hawaii is dramatically near sided with intermediate VGPs which closely straddle the site meridian. This finding, together with the weak relative remanence intensities associated with the excursion⁵, further justify the claim that aborted reversals exist in the palaeomagnetic record and, moreover, are identifiable.

The remaining excursion data displayed in Fig. 1 correspond to records obtained from sites in the Southern Hemisphere. As with the Northern Hemisphere record, these three VGP paths are clearly found to be either near sided or far sided. In fact, it is

the single record corresponding to a reserve polarity excursion (Fig. 1, lower right) which is near sided while the two normal polarity excursions (Fig. 1, lower left) are far sided. Hence, all excursions which qualify as possible aborted reversals show intermediate VGP behaviour consistent with the finding in regard to transitional field geometries that non-dipole axisymmetric component(s) predominate. Moreover, the clear categorization of near-sided and far-sided paths by site locality and polarity state (during excursion) suggests that certain systema-

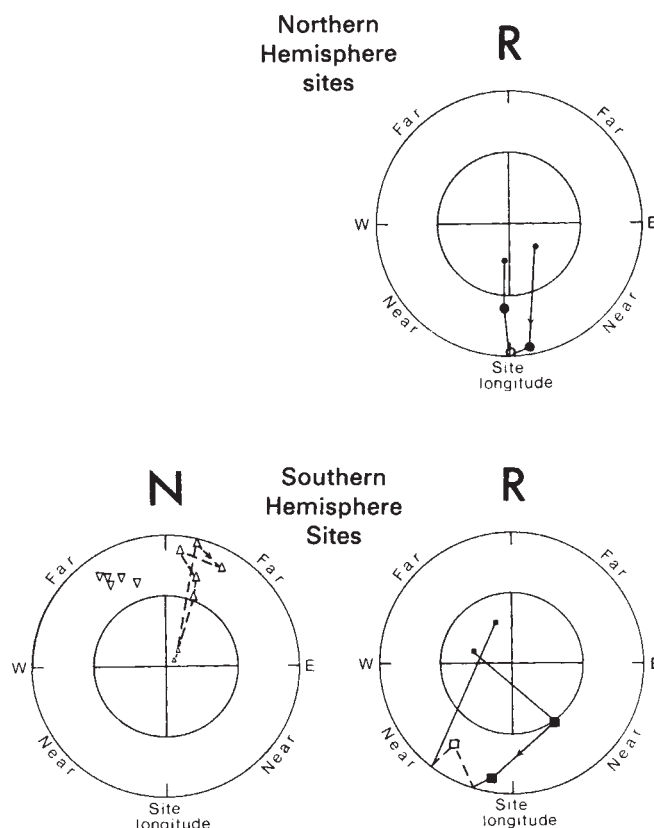


Fig. 1 Polar stereographic projections of VGPs from data sets listed in Table 1 and plotted with respect to site longitude. Each excursion is plotted separately depending on the hemisphere of the recording site and the full polarity state (N, normal; R, reverse) at the time of occurrence. Circles representing 45° latitude and the Equator are drawn in each case. Open and solid symbols (see also Table 1) represent Northern Hemisphere and Southern Hemisphere VGPs respectively. The Amsterdam Island data are shown without a path as a strict succession of flows was not presented in the literature⁶.

tics of the aborted reversal process exist. In fact, when these excursion data are combined with available detailed transition records⁹, a consistent set of VGP characteristics is obtained. Independent of the hemisphere in which the records were obtained, reverse polarity excursions and R→N transitions are associated with near-sided VGP behaviour whereas normal polarity excursions and N→R transitions are associated with far-sided VGP behaviour. These findings, listed by Hoffman and Fuller¹² as one possible regime, correspond to a predominantly quadrupolar (g_2^2) intermediate field geometry⁸.

The finding that the VGP systematics depend on the sense of reversal supports the hypothesis that transitional fields are a result of the configurational characteristics of the reversal process in the core¹²⁻¹⁵. Moreover, these data are consistent with the idea that reversals have their origin in the Southern Hemisphere of the core. The hypothesis that a significant long-term standing (non-reversing) field exists during reversal attempts^{16,17} is not supported, although a stationary field of short duration⁷ cannot be excluded.

Thus four records of palaeomagnetic excursions from low- to mid-latitude sites satisfy stringent criteria for reliability. Although few, these recordings display corresponding VGP behaviour which is constrained in longitude. Moreover, for each case, the path locality of the intermediate VGPs is unambiguously either near sided or far sided with respect to the longitude of the recording site. The single acceptable reverse polarity excursion from the Northern Hemisphere displays field behaviour consistent with that observed during R→N transitions also recorded at northern latitudes. These findings support the hypothesis that at least some geomagnetic excursions are aborted reversals and therefore the palaeofield variations derived from such records can be interpreted as transitional field behaviour. The intermediate VGP data (associated with the four acceptable excursion records), together with those from successful reversals, support the hypothesis that the controlling axisymmetric component of transition fields is quadrupolar. They also support the idea that the geomagnetic reversal process initiates in the Southern Hemisphere of the core. Why such an apparently symmetric entity as the Earth's outer core should be associated with an asymmetric reversal initiation process is debatable. The hypothesis of a long-term stationary, non-reversing field which controls the geometry during polarity transition attempts is not supported by these data. It remains to be seen whether additional palaeomagnetic records of either successful or aborted reversals will continue to support these conclusions.

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Lower Proterozoic arc-microcontinent collisional tectonics in the western Churchill Province

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Arguments favouring evolution of the 'Hudsonian' orogen of the Churchill Province through plate tectonic processes¹⁻³ are generally supported by recent work in Saskatchewan and Manitoba⁴⁻¹¹. Palaeomagnetic data do not preclude operation of the Wilson cycle in this region during the Lower Proterozoic¹²⁻¹⁵. At present, however, subduction-related sutures in the Churchill Province are unconvincingly documented. Even the Thompson Belt ('Nelson Front'), forming part of the postulated suture between the Superior Province craton and the western Churchill mobile belt (Fig. 1), is markedly oblique to major volcanoplutonic and other lithostructural belts of the western Churchill and is thus unlikely to be a simple collisional junction. Orogens formed at consuming plate margins are likely to incorporate pre-terminal, arc-related sutures, variably obscured by later events¹⁶. Previous proposals for location of such intra-orogenic sutures within the western Churchill belt, predicated largely on geophysical evidence¹⁷, are unsupported by recent geological investigations⁵. However, on the basis of recent fieldwork, I now outline a strong geological case for intra-orogenic collisional suturing and microplate interaction in south-east parts of the Churchill Province in Saskatchewan.

Six major lithotectonic elements can be distinguished (Fig. 1).

(1) The Rottenstone-La Ronge Magmatic Belt, developed at the south-east margin of continental crustal terrain, represented by the Cree Lake Zone⁵, is a Hudsonian 'Cordilleran-type' arc massif^{6,10}. Most of the belt comprises the plutonic core of the arc: subordinate calc-alkaline, arc-type (Watters, personal communication) volcanics-volcaniclastics are preserved mainly in south-east parts of the belt. There is markedly asymmetric distribution of plutonic rock types¹⁰, with dominant quartz monzonite-granite-granodiorite in the north-west and calc-alkaline quartz diorite-tonalite-granodiorite in the south-east.

(2) The eastern La Ronge domain, a metasedimentary belt up to 20 km wide, mostly comprises quartz-plagioclase-biotite psammites and semipelites interlayered with, and transitional to, calcareous hornblende/diopside psammites, hornblende gneisses and amphibolites^{18,19}. Pebbly psammites and immature polymictic conglomerates form thin layers up to major units in, and locally transitional to, both psammites and hornblende gneisses. These rocks are interpreted as volcanogenic proximal greywackes, volcanoclastic-epiclastic sediments with minor lavas, and submarine fan deposits, derived from the Rottenstone-La Ronge arc. Both arc volcanics and derived sediments are stratigraphically overlain by locally conglomeratic arkoses preserved within an overturned disrupted synform on the western margin of the sedimentary belt.

The domain is affected by at least two deformation events which produced coplanar, north-east-trending isoclinal folds, foliation, limb-sliding and thrust stacking. These structures are deformed by open folding about north-trending axial surfaces. Strain indicators suggest extreme flattening normal to early foliation and fold axial surfaces, with very high extensional strains in the downdip direction.

On the basis of location, lithology and deformation, the eastern La Ronge domain is interpreted as the severely telescoped remnants of a forearc basin.

(3) Most of the Glennie Lake domain comprises early quartz dioritic-granodioritic orthogneisses and later foliated to undeformed dioritic to granitic plutons. Subordinate supracrustals occupy narrow arcuate belts within the orthogneisses: in the

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north-west they are in part continuous with, and similar to, supracrustals of the eastern La Ronge domain; elsewhere they include more abundant volcanics.

The domain has distinctive structural character. Early orthogneisses and supracrustals possess initially flat-lying gneissic foliation, isoclinal folding and lineation resulting from at least two deformation events. In the north-west, major recumbent folds can be correlated with more steeply overturned D_2 isoclines of the Eastern La Ronge domain. These nappes are refolded by large wavelength, open to tight, north-trending D_3 , and north-east-trending D_4 folds, producing type 1 interference patterns. Differences in lithological character and structural succession in adjacent supracrustal zones²⁰ may result from juxtaposition of autochthonous and allochthonous elements.

Most documented thermotectonic and plutonic events in the Glennie Lake domain are probably Hudsonian: limited Rb/Sr whole-rock dating (K. Bell and J. Blenkinsop, personal communication) has to date yielded no pre-Hudsonian ages. Nonetheless, lithostructural character and the nature of domain boundaries indicate that the domain possesses fundamentally different basic crustal structure and evolution compared with adjacent domains.

The south-west part of the La Ronge–Glennie Lake domain junction is defined by the 2–4 km wide Stanley Shear Zone¹⁸ which incorporates submylonitic and blastomylonitic gneisses interpreted, on structural and metamorphic evidence, to have developed early in local thermotectonism. To the north-east, this early 'straight belt' disappears and the Stanley Zone is marked only by late dextral strike-slip faults, across which broad

continuity of lithology and structural trends occur. Even here, however, the domain junction is marked by major changes in fold style and attitude.

(4) South of Reindeer Lake, the Tabernor Zone is a narrow 'straight belt' with a complex history dating from early- and possibly pre-Hudsonian time. It includes blastomylonitic gneisses formed early in Hudsonian thermotectonism^{21,22}, tightly appressed northerly-trending folds and syn- to post-metamorphic faults. The zone is marked by a pronounced metamorphic gradient^{21,23}. The southern part of the zone was thus a fundamental crustal dislocation active throughout Hudsonian orogeny.

To the north, the Tabernor Zone changes abruptly in character and documented history as it extends across the Rottenstone–La Ronge belt, marked most obviously by splaying of the shear zone into a broader, diffuse set of fractures. The latter are associated with late Hudsonian open northerly folds in the La Ronge domain but these disappear farther north and the Tabernor system is thereafter characterized only by brittle faults with sinistral strike-slip displacement. All early Hudsonian phenomena disappear as the Tabernor Zone leaves the Glennie Lake–Kisseynew terrain.

(5) The Kisseynew domain mostly comprises highly migmatized, proximal to distal volcanogenic metagreywacke turbidites, subordinate metavolcanics and arkoses^{7,24}. Interdigitating facies relations with supracrustals of the La Ronge–Lynn Lake and Flin Flon–Snow Lake volcanoplutonic arcs are well documented and the 'Kisseynew Gneisses' are generally interpreted as being deposited in part contemporaneously with arc development. Original continuity between the northern Kisseynew terrain and the eastern La Ronge forearc seems certain.

Most granitoids of the Kisseynew domain are locally derived anatectites. Major Hudsonian plutons are uncommon, except adjacent to the La Ronge and Flin Flon belts. Older 'basement' is recorded only immediately east of the Tabernor Zone, in the south-west part of the domain: the Sahli Granite is dated at $2,430 \pm 30$ Myr (Rb/Sr whole rock isochron)²⁵ and volcanics and granitic rocks in the Hanson Lake area at $2,521$ and $2,446 \pm 16$ Myr (Rb/Sr whole rock isochrons)²⁶. Rocks of the latter area are akin to those in adjacent parts of the Glennie Lake domain and provide tenuous geochronological indication of possibly extensive older continental basement in the latter.

(6) The Flin Flon domain (and its extension, the Snow Lake belt of Manitoba) is a well documented Lower Proterozoic arc complex^{27–29} similar in most respects to the Rottenstone–La Ronge Magmatic Belt. Age data indicate that the two arcs are essentially coeval but suggest the Flin Flon arc could be slightly younger³⁰.

The Glennie Lake domain has previously been interpreted, speculatively, as incorporating pre-Hudsonian continental crust^{6,11,18}. While this is unconfirmed by radiometric data the domain possesses distinctive lithostructural style and is bounded largely by major tectonic discontinuities. Metamorphic data strongly emphasize domain contrasts and support interpretation of the Tabernor Zone as a fundamental crustal feature. Interpretation of the Glennie Lake domain as possessing radically different pre-Hudsonian crustal character, relative to adjacent domains, provides a possible explanation of regional geology and gross structural geometry, and accords with a general model for Hudsonian evolution in the southeastern Saskatchewan–Manitoba Shield.

It is thus argued that in early- to mid-Hudsonian time the Glennie Lake domain formed a microcontinental block within a dominantly oceanic lithospheric plate which was subducting beneath the Rottenstone–La Ronge arc along a consuming plate margin located south-east of the eastern La Ronge–northern Kisseynew terrains (Fig. 2a). This resulted in collision of the Glennie Lake block with the eastern La Ronge forearc and ensuing arc–microcontinent suture (Fig. 2b). The collision produced extreme telescoping of the forearc prism, locally leading to almost complete squeezing out, at the present erosion

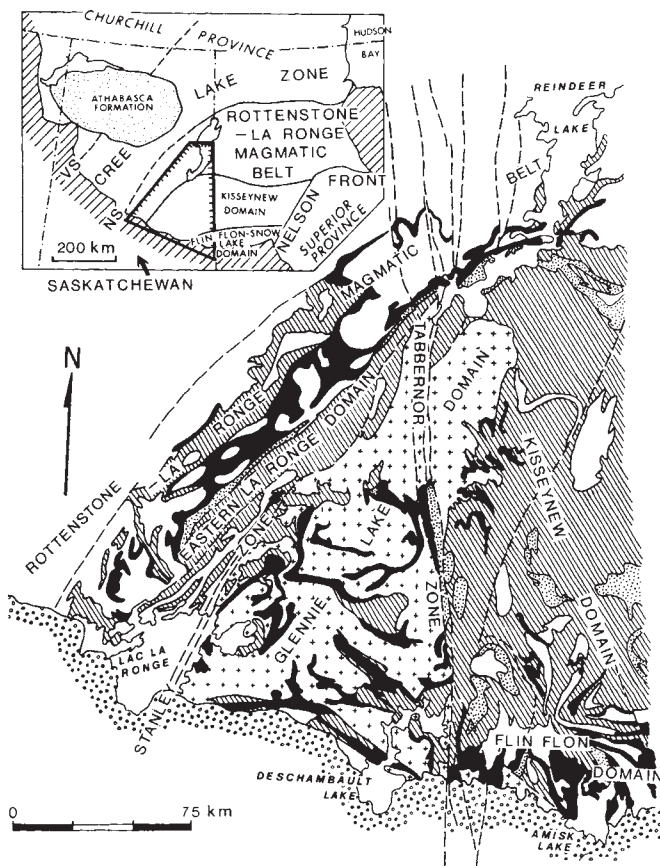


Fig. 1 Geology of the southeastern part of the Churchill Province in northern Saskatchewan (location indicated by heavy, hatched lines in inset). Solid black area, undifferentiated metavolcanics; ▨, mainly volcanogenic metasediments; ▩, meta-arkoses; ▧, undifferentiated granitoids of Glennie Lake domain and Hanson Lake area; unshaded area, quartz dioritic to granitic plutons of other domains; ▨, Phanerozoic cover (oblique line in inset). Dashed lines indicate fault and shear zones. VS (inset), Virgin River Shear Zone; NS (inset), Needle Falls Shear Zone.

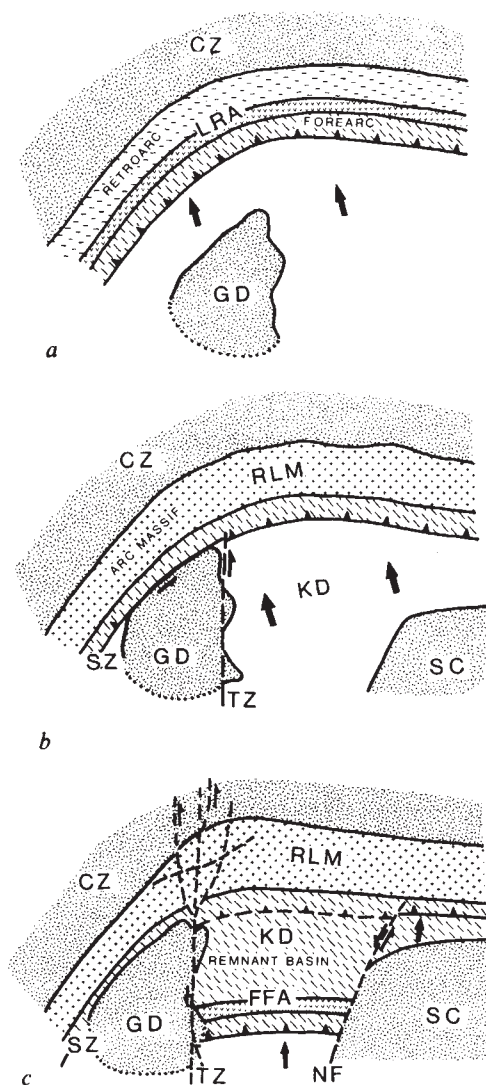


Fig. 2 Possible tectonic evolution of the south-east Churchill Province in Saskatchewan and Manitoba. *a*, (~1,950–1,900 Myr?): early Hudsonian development of subduction zone and La Ronge-Lynn Lake volcanic arc marginal to Cree Lake continental margin. The Glennie Lake domain is an 'outboard' microcontinent within a predominantly oceanic subducting plate. *b*, (~1,900–1,870 Myr?): collision of Glennie Lake domain with eastern La Ronge forearc and initial telescoping of the forearc prism. Uncoupling occurs between the impeded Glennie Lake microplate and still subducting Kisseynew microplate with initiation of the southern Tabernor Zone. The arc is uplifted and stripped to form a major Cordilleran-type arc massif, the Rottenstone-La Ronge Magmatic Belt. The Flin Flon-Snow Lake arc may be initiated by migration of subduction site southwards between the Tabernor and Thompson 'transforms' or may already have been active in the outboard part of the southern plate. *c*, (~1,860 Myr?): the Glennie Lake domain is sutured to the arc massif with immense telescoping of the forearc and possible transcurrent reactivation along the suture. Subduction north of the Kisseynew domain has ceased and the suture buried beneath sediment influx. The Kisseynew subplate becomes an interarc remnant basin receiving sediments both from north and south. Differential movements propagate the Tabernor Zone northwards as a splaying wrench system. The Thompson Belt forms another transcurrent/transform junction, to the east of which incoming of the Superior continent leads to terminal collision along the northern part of the Nelson Front, followed by general compression, late folding, continuing propagation and reactivation of major fractures. Assigned dates are speculative, based on limited radiometric data. CZ, Cree Lake Zone; GD, Glennie Lake Domain; SC, Superior Craton; LRA, La Ronge-Lynn Lake Arc; FFA, Flin Flon-Snow Lake Arc; RLM, Rottenstone-La Ronge Magmatic Belt; KD, Kisseynew Domain; SZ, Stanley Zone; TZ, Tabernor Zone; NF, Nelson Front (Thompson Belt).

level, of forearc sediments between the arc massif and microcontinent. Deformation and indicated bulk strain in the forearc belt are consistent with this interpretation. Recumbent fold/thrust sheets were driven southeastwards out of the forearc across the advancing microcontinent. In part, such nappes may include thrust slices from the leading edge of the microcontinent. The Stanley Shear Zone is thought to represent, not the actual collision suture, which is presumably overridden, but the main sole zone of detachment of allochthonous sheets moving over the Glennie Lake block. Farther north this detachment zone is folded and plunges beneath the allochthon.

Further deformation in the Glennie Lake domain, accompanying final collision stages (and possibly related also to new or continuing subduction to the east or south) resulted in major refolding of autochthonous basement and allochthonous cover, accompanied and outlasted by plutonism. Reactivation along the suture zone produced later faulting which extended into the overriding allochthon, thus generating the presently exposed north-east part of the Stanley fault system.

The Tabernor Zone is interpreted as a transform junction initiated between the Glennie Lake microcontinent and the Kisseynew subplate (which may be underlain by predominantly oceanic lithosphere). Uncoupling along this zone is thought to have accompanied locking up of the Glennie Lake block in relation to still subducting lithosphere underlying the Kisseynew domain (Fig. 2c). Though the Tabernor Zone generally conforms to the Glennie Lake domain junction it seems that prominences were detached as fragments within the dominantly oceanic subplate, as, for example, the Hanson Lake block.

The Kisseynew basin was filled with detritus from the La Ronge-Lynn Lake and Flin Flon arcs, which may have been active simultaneously for a time: alternatively, the Flin Flon arc may be younger and result from rapid migration, or jump, of the subduction site along the transform junction. Resolution of these alternatives awaits more refined stratigraphic mapping and radiometric dating. The subduction zone related to the eastern part of the La Ronge-Lynn Lake arc is thought to be buried beneath Kisseynew basinal sediments.

The Flin Flon-Snow Lake arc is bounded by the Tabernor Zone to the west and the Thompson Belt to the east: the latter is interpreted as another major transform, or transcurrent, junction between the Kisseynew subplate/remnant ocean basin and Superior continental craton. Northerly subduction beneath the arc is invoked to explain high grade metamorphism of the Kisseynew terrain, as compared with the southern Glennie Lake domain and Superior craton.

Stresses induced in the already crystalline Rottenstone-La Ronge arc massif and Cree Lake Zone, due to differential activity of segments of the subducting plate, are postulated to have caused northwards propagation of the Tabernor Zone across the underthrust continental plate as a splaying wrench system. Further propagation and reactivation accompanied late-Hudsonian terminal collision and overall compression, producing sinistral displacements along the Tabernor Zone and reactivation of other major discontinuities such as the Stanley Zone.

The proposed model accounts for hitherto unexplained differences in character of northern and southern parts of the Tabernor Zone and its oblique orientation relative to other elements of the western Churchill Province. It provides a viable explanation of the 'aberrant' orientation of the Thompson Belt in plate tectonic modelling of the Hudsonian orogen.

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Volcanic components in pelitic sediments

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The origin of the clay minerals present in pelitic sediments has been widely debated. Weaver¹ suggests that illite and interstratified illite/smectite (I/S) dominate. The association of illite with marine sediments² and the proposal^{3,4} that illite forms from smectite (an expandable clay mineral sometimes referred to as montmorillonite) in the marine environment has also been discussed. Weaver⁵ argues for a continental origin of illite, produced by weathering of K-feldspar. Others^{6–9} have shown that smectite and I/S (20–50% illite) are converted to I/S of higher illite content (60–80%) in pelitic sediments by low-grade metamorphism. Per cent illite will always refer to the per cent illite in I/S. The designation should not be confused with the content of discrete illite or mica commonly present in these sediments. Here we present clay mineral and K–Ar data for Cretaceous marine shales from the Western Interior of North America demonstrating a volcanic origin for much of these sediments. This observation is correlated with eustatic sea-level rise, increased volcanic activity, sedimentary preservation of organic matter, and incorporated into a petrogenetic/tectonic model for pelitic sediments.

It has been shown^{8–10} that Cretaceous marine sediments from the Western Interior of North America are primarily composed of random I/S¹¹. In some areas, the clay mineral assemblages of these sediments have been converted to ordered I/S^{8,9} and illite by low-grade metamorphism. Unpublished X-ray diffraction data of contact metamorphic Cretaceous clay mineral assemblages in the Spanish Peaks area, Colorado, clearly demonstrates that the I/S is converted to 100% illite. Fine-grained, vitreous, volcanic debris is generally accepted as the source of the smectite clay^{1,12}. The presence and resulting mineralogy of numerous bentonites¹³ associated with these sediments supports this interpretation. I/S clay mineral data from 77 bentonite-shale sample pairs in the Cretaceous Mancos shale are shown in Fig. 1. Excellent agreement between the nature of interstratification of the sample pairs is indicated. Although the bentonites order before the shales, the per cent illite is generally higher in the shales, particularly for those sample pairs of random interstratification (Fig. 1). Schultz¹⁰ has noted a similar discrepancy and proposed that this greater amount of illite in shales compared with bentonites may be related to longer marine residence times of volcanic debris and consequent alteration to random I/S in the resulting shales. High sedimentation rates of volcanic debris, resulting in the formation of

Table 1 K–Ar age determinations of clay size fractions from Cretaceous marine shales

Sample	Potassium-bearing clay mineral	Age (Myr)
MS921	Randomly interstratified illite/smectite (I/S), 50% illite	98.3 ± 4 (Upper Cretaceous)
MS86	Discrete illite	2.3 ± 8 (Triassic)

distinct bentonite beds, have a much shorter marine residence time and are therefore essentially smectitic. Consequently, bentonite–clay alteration occurs primarily below the sediment–water interface, and may explain the very low illite content of I/S in bentonites. We agree with this interpretation. However the similarity in clay mineralogy of non-marine and marine Cretaceous pelitic units may indicate a continental role in the formation of random I/S from volcanic debris (L. G. Schultz, personal communication). This point is important because the location of clay potassium adsorption, and consequent formation of illite, has major implications with regard to the chemical cycle and distribution of potassium in the lithosphere and hydrosphere. For this discussion, we contend that despite the discrepancy in illite contents of I/S, the gross similarity of the clay mineralogy of Cretaceous shales and bentonites, particularly with regard to the nature of interstratification, suggest a common origin, that is, the result of alteration of volcanic debris.

K–Ar investigations of pelitic sediments, which are primarily concerned with the dating of illite, the major potassium-bearing phase, have produced complex results¹⁴ that are partly due to the mixing of detrital illite derived from older lithologies and younger metamorphic illite^{15,16}. Similarly, K–Ar interpretation of the Cretaceous shales is complicated by the presence of minor amounts of discrete illite in almost all the clay size fractions of the samples. However, a few shales were found to have clay size fractions composed of either random I/S or pure discrete illite. K–Ar determination of these samples (Table 1) indicate that the discrete illite (MS86) is probably detrital from an older source (213 Myr), that is, pre-Cretaceous, whereas the random I/S (MS921) yields approximately the correct stratigraphic age (98 Myr). Additional evidence is provided by the K–Ar investigation of Hoffman¹⁷ on Missouri River sediments in which Cretaceous shales are the major stratigraphic units in the drainage basin. In this study, clay minerals from 11 sediment samples, essentially random I/S, yielded ages of 79–125 Myr averaging ~100 Myr. Bentonites, on the other hand, often contain no detrital sedimentary components. If the original smectite in bentonites is converted to ordered I/S, there is little doubt that the measured age records potassium fixation and

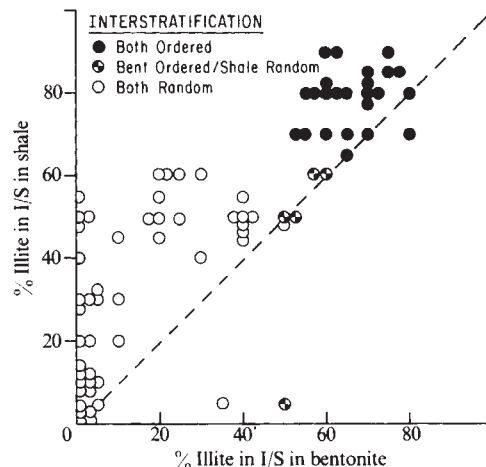


Fig. 1 Relationship between percentage illite in interstratified illite/smectite (I/S) from bentonite–shale sample pairs (equivalents line (broken) is shown for comparison).

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consequent illite formation during burial or contact metamorphism¹⁶. Five samples of such bentonite materials were dated by K-Ar methods, and produced ages between 62 and 40 Myr (ref. 18). The clay from shale that has the correct stratigraphic age (98.3 Myr) could be produced by a mixture of discrete illite and ordered I/S, however, no trace of either discrete illite or ordered I/S was resolved by X-ray diffraction. A simple calculation shows that sufficient 200-Myr material is needed to increase a 60-Myr age to 100 Myr producing a mixture in which discrete illite would have been clearly resolved in the diffraction pattern. We therefore conclude that the 98.3-Myr random I/S is a mineral phase whose potassium content was fixed at or near the time of Cretaceous sedimentation, hence supporting the contention that random I/S represents first-cycle sedimentary material resulting from the alteration of volcanic debris. Hoffman¹⁷ drew similar conclusions from his age data.

The Cretaceous is an unusual period in several respects. The proliferation of epicontinental marine sediments due to a high stand of eustatic sea level during this period produced marine transgressive sedimentary sequences on almost all the continents^{19,20}, including the invasion of marine depositional environments into the Western Interior of North America. Gilluly²¹ shows the difficulty in providing a detrital source area for the Cretaceous marine sediments of North America (volume = 4×10^6 km³). Based on particle size and quantitative clay mineral analyses of the Cretaceous Pierre shales, I/S represents ~38% of the total sediment²². From a comparative study of coarser size fractions of the Pierre shales with those of bentonites Jones²³ estimates that ~40% of these sediments are the result of pelagic deposition of aeolian transported volcanic debris. Therefore, the data indicate that approximately one-third to one-half of these sediments are of volcanic origin, possibly explaining the difficulty in reconciling their source from reworked older rocks. The influx of volcanic material into the Cretaceous marine environment was episodic, and at times completely dominated the sedimentation as evidenced by the presence of numerous bentonites. This form of sedimentation is characterized by relatively uniform sediment accumulation over much of the basin and is much different from that of fluvial deltaic systems that localize sediment in more restricted depositional environments. Petrologically, the Cretaceous shales have many features in common with black shales elsewhere. The depositional environments resulting in the formation of black shales are of great interest because of their association with hydrocarbon and some types of metallic ore deposits. Factors important in their formation are organic productivity, sedimentation rate, and rate of oxidation of organic matter before burial^{24,25}. The volcanic-sedimentary episode may have had other geochemical consequences, such as the influx of chemical elements into the atmosphere and oceans from volcanic ash and gases. These factors may provide a conducive environment for the formation of black shales. Organic-rich pelagic sediments were preserved globally in various marine environments during the Cretaceous^{26,27}. These 'anoxic events' have been correlated with the rise in eustatic level, increases in organic production and changes in global climate. Scholle and Arthur²⁸ have shown that the ¹³C isotopic composition of Cretaceous carbonates increases from 120 to 80 Myr, reaching a maximum at 108 Myr. This increase in ¹³C is correlated with the increased preservation of organic matter in these sediments. Other studies^{29,30} have shown a dramatic 3-4-fold increase in the rate of seafloor spreading (up to 18 cm yr⁻¹) during the mid-Cretaceous (110-85 Myr), and that there is a direct relationship between the rate of spreading and eustatic sea level. Kauffman³¹ has noted a correlation between emplacement of calc-alkaline batholiths and bentonite frequency in marine sediments, suggesting a link with tectonic activity. McBirney³² observed a relationship between marine transgressions and episode volcanic activity which tends to be synchronous over a broad region of the Earth. All the evidence suggests that these dynamic Earth processes are related. The record of high eustatic sea level would correspond to periods of higher volcanic activity, the debris from which

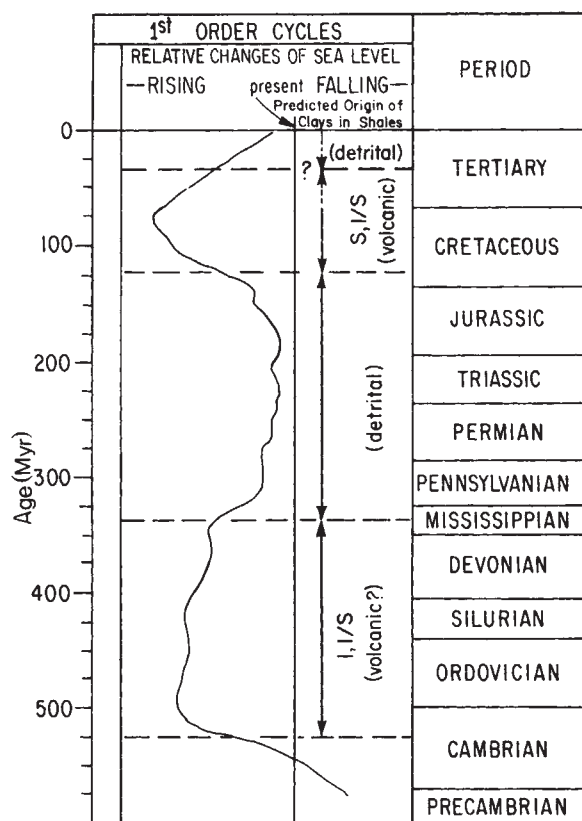


Fig. 2 Eustatic sea level²⁰ and clay petrology of pelitic sediments (mainly after ref. 1) throughout the Phanerozoic. I, illite; I/S, interstratified illite/smectite; S, smectite.

accumulates in the greatly expanded marine environment, readily altering to smectite and random I/S.

This discussion may be relevant to the origin of the bulk of clay minerals preserved in pelitic sediments. Are there any analogues to this form of sedimentation proposed for the Cretaceous? Some cases of the lower to mid-Palaeozoic systems of eastern North America are good candidates, given the proliferation of marine sedimentation, the widespread occurrence of Ordovician and Devonian bentonites, and the formation of black shales. In Weaver's¹ classic work on the clay petrology of sediments, he notes that the dominant clay mineral present in pre-Upper Mississippian sediments is illite and I/S. Here again a discrepancy exists between the clay mineralogy of Palaeozoic bentonites, which are I/S, 80-90% illite, and shales which contain I/S that is generally 90% illite, and illite. In the Cretaceous sediments, I/S in the shales have a higher illite content than do the bentonites, and should this lag in illite content continue through higher grades of burial metamorphism, the I/S of shales would be expected to convert the 100% illite before the I/S of the bentonites. Given the relationship of eustatic sea level and volcanic activity, inspection of Fig. 2 predicts that much of the illite and I/S of these sediments may represent the accumulation of volcanic debris, originally in the form of nearly pure smectite and random I/S, later modified by metamorphic conversion of smectite to illite. Periods of low eustatic sea level would be predicted to have a lower overall volcanic influx, allowing the reworked detrital influx to dominate. The abundance of pelitic sedimentary and metamorphic rocks, which make up more than half of the sedimentary record³⁴ in continental source areas, combined with the stability of phyllosilicates in aqueous systems are in part responsible for their presence in detrital clay mineral assemblages. Therefore, incorporation of older, volcanically derived clay into later depositional environments is a common occurrence. The Clay mineral assemblages of the Upper Palaeozoic and Lower to Middle Mesozoic^{1,2}, as well as Recent marine sediments³³, are in fact, highly variable in composition and lack

the uniformity of the lower to mid-Palaeozoic and most of the Cretaceous.

We have tried to rationalize many different facts and hypotheses for the Cretaceous sedimentation in North America. A major marine transgression was accompanied perhaps by increased volcanic activity at the subduction zones. Clay mineral and K-Ar data from Cretaceous shales suggest that the smectite and I/S which are major components in these sediments are derived primarily from volcanic debris. Thus one model exists that explains the aqueous environment for the accumulation of a sedimentary record, and the volcanic sources to fill it. Illite, I/S and smectite are the dominant clay minerals in pelitic sediments. The similarity between clay mineral assemblages of Lower to Middle Palaeozoic marine shales with the inferred mineralogy of Cretaceous marine shales after deep and prolonged burial suggests that the Cretaceous model described above may be general, and that the derivation of smectite and random I/S from volcanic debris and its later metamorphic conversion to ordered I/S and illite is a major reaction sequence affecting the clay petrology of pelitic sediments.

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The rock samples in which the microfossils were found were collected from the middle member of the Dengying Formation and from the lower member of the Meishucun Formation of the Sinian 'system' the Wangjiawan and Meishucun sections (Fig. 1). The carbonaceous rocks of the upper member of the Meishucun Formation at both sections (W. and M.) have been dated to 603 ± 31 Myr and 612 ± 36 Myr respectively (by Rb-Sr isochron dating where $\lambda^{87}\text{Rb}$ is 0.142 yr^{-1}). The fossiliferous area of the Meishucun Formation in the Wangjiawan section is more than 60 m below the oldest trilobite-bearing beds of the Lower Cambrian and about 15-20 m above the lowest occurrence of small shelly fossils. The stratigraphical position in the Meishucun section is more than 50 m below the oldest trilobite-bearing beds. The fossiliferous bed of the Dengying Formation of the Wangjiawan section is more than 100 m below the lowest beds containing small shelly fossils. The fossiliferous rocks consist of non-stromatolitic chert laminae or lensed bodies (nodules) which form intercalated beds in dolomite or dolomitic fine-grain sandstone.

The type of microfossil preserved in the cherts of the Wangjiawan section is the same as that previously reported for Precambrian deposits; however, the microfossils from the cherts of the Meishucun section are strongly mineralized, light in colour and partially or totally lacking in organic matter, so that they can only be considered as fossils on the basis of their apparent biological nature. Secondary silification may be a good process for preserving microfossils originally mineralized after death.

The Dengying and Meishucun microfossil assemblages are morphologically of three forms—spheroids, trichomes and sheath-like filaments. Most of the coccoids and filamentous forms are well preserved. Although most of the fossils are degraded forms and lack detailed structure, their morphology, size range and the cell structures occurring randomly in some of the samples enable their classification either as a previously described Precambrian taxon or as a new genus or species.

Among the coccoids, the colonies shown in Fig. 2f are assigned to *Clonophycus* Oehler², which have been compared with large cells of eukaryotic green or red algae; those in Fig. 2e, g are assigned to *Myxococcoides kingii* Muir³; and the samples shown in Fig. 2n may be a new taxon of non-ensheathed colonies composed of unicells which occur in individual spheroids, in pairs or in planar tetrads, and are 7-22 μm in diameter (commonly 11-16 μm), with a psilate surface texture, but no sheath or organic matrix. Both the known taxa can be compared with members of the Recent *Chroococcaceae*. Samples of solitary unicells (Fig. 2a-c) are assigned to *Myxo-*

Sinian microfossils from south-west China

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The microfossil assemblages described here are preserved in cherts from the Yunnan Province, south-west China. They are the first chert-facies microfossils to be discovered in the Wangjiawan and Meishucun stratigraphical sequences which are regarded by the International Cambrian/Precambrian Boundary Working Group¹ as possible 'candidates' for the stratotype section of the Cambrian/Precambrian boundary.

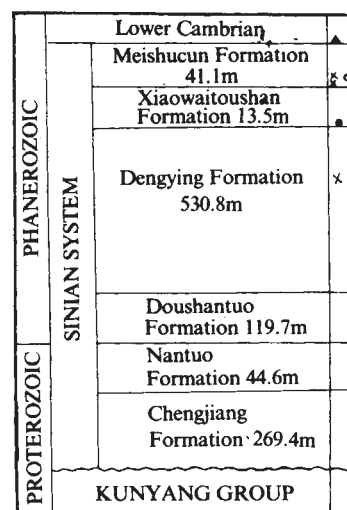


Fig. 1 Stratigraphy of the Sinian System in Yunnan Province, China, showing the occurrence of fossiliferous chert samples from the Wangjiawan section (×), the Meishucun section (○), and the oldest trilobite bed (▲) and lowest bed containing small shelly fossils (●) in Wangjiawan section.

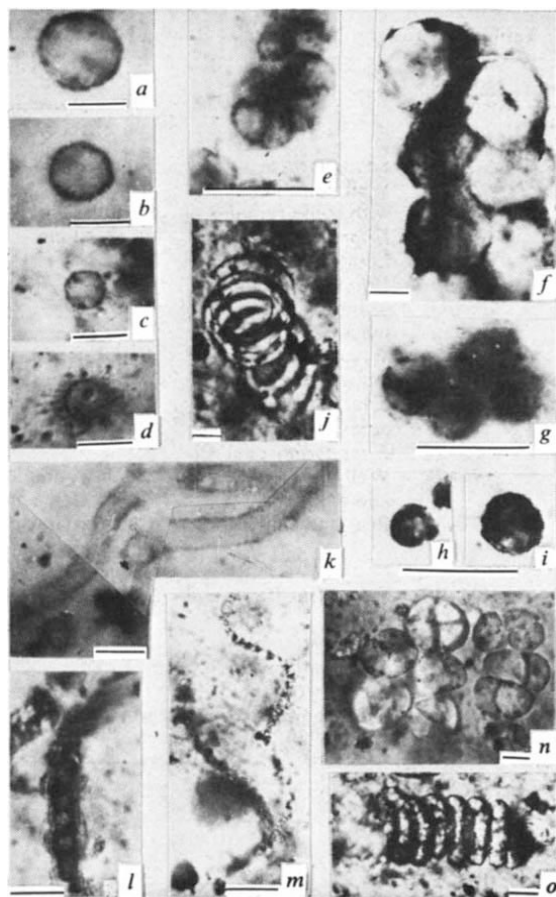


Fig. 2 Optical photomicrographs of the Sinian fossils discovered in chert thin sections from the Meishucun Formation (a-e, g-i, k) and the Dengying Formation (f) of the Wangjiawan section, and from the Meishucun Formation of the Meishucun section (j, l-o). Scale bar, 10 μm .

coccoides grandis Horodyski & Donaldson⁴. Spheroidal envelopes (or round flattened membranes) (Fig. 2h, i), which closely resemble acritarcha fossils obtained by simple palynological methods from Precambrian sediments, are of the taxum *Protosphaeridium* Timofeev⁵. Several coccoidal unicells with radial setaceous spines (Fig. 2d) were discovered in the cherts of the Meishucun Formation from the Wangjiawan section; they resemble members of acritarcha *Baltisphaeridium* discovered in Russian Cambrian sediments by macerating rock⁶, and are 6.5–7 μm in diameter, with spines <0.5 μm wide and 2.5–5 μm long.

In some thin sections of chert from the Meishucun Formation of the Wangjiawan section only one kind of non-septate filament (Fig. 2k) has been discovered which has been assigned to *Eomycetopsis robusta* Schopf emend Knoll & Golubic⁷. This taxum includes structures resembling the empty sheath of cyanophitic or bacterial trichomes. Other sections from the same formation contain extensively degraded non-septate filaments of this taxum (Fig. 2m) together with an abundance of several other kinds of filament. Those shown in Fig. 3h, i are of the species *Cyanonema inflatum* Oehler²; comparable with the recently discovered member of Oscillatoriaceae; the coiled filaments shown in Fig. 2j, o are assigned to the *Obruchevella parva* Reitlinger⁸ and comparable with recently discovered cyanophitic blue-green alga *Spirulina*. The sample illustrated in Figs 2l and 3a–g, j may be a new taxon.

The filaments shown in Fig. 3f, g appear to be unbranched, uniseriate, septate and multicellular and resemble *Cyanonema inflatum* except for the occurrence of a thin sheath and some larger cells that may be heterocysts (?) typical of the Nostocaceae. The specimens shown in Fig. 3e seem to be degraded

trichomes of uniseriate, septate, multicellular filamentous algae, although the filaments have indistinct outlines; the septate filaments can also be seen in the well preserved larger cells (which may be heterocysts) distributed along the filament. The trichomes are ~3–4 μm in diameter, and the larger cells 4–5 μm wide and 4.5–6.5 μm long; each of the larger cells contains a black body, 1–2 μm in diameter, irregular or oval in shape and comprised of degraded cellular matter. The specimens are similar to members of the genus *Veteronostocale*⁹, which has been compared with recently found Nostocaceae; however, they are unnamed here because of their poor state of preservation.

The larger filaments discovered are shown in Fig. 3a–d, j; all resemble recently discovered members of Oscillatoriaceae, being unbranched, uniseriate, septate and multicellular or non-septate tubular, disk-like trichomes with a distinct sheath. Figure 3a shows an ensheathed trichome; such trichomes occur as a coiled filament 26–30 μm in diameter, as a round coiled body 250 μm in diameter, or as disk-like medial cells, 3–8 μm long and 26–28 μm wide. The samples may represent fragments of a larger member of the *Obruchevella*, or a new taxon not yet described, and are tentatively named here *Circulinema jinningense* gen. et sp. nov. on the basis of their preserved state. The coiled filaments shown in Fig. 3b–d resemble *C. jinningense* except for their lack of internal cells; they occur in non-septate form are 19–21 μm in diameter and coil to give bodies 73–140 μm in diameter; this type of coiled filament may represent the empty sheath of *C. jinningense* or the degraded form of the latter which have few or no internal cells because of degradation. Figure 3j shows a fragment of a larger member of the Oscillatoriaceae, 27–28 μm in diameter, with a distinct sheath and disk-like medial cells.

The Sinian microfossils described here are of interest in Precambrian microbial study because: (1) although other Pre-

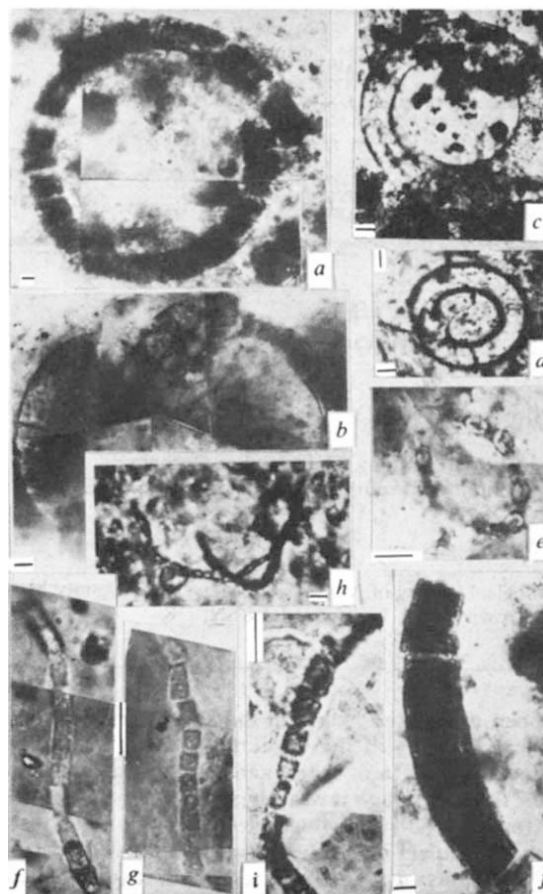


Fig. 3 Optical photomicrographs of the Sinian fossils discovered in chert thin sections from the Meishucun Formation of the Meishucun section. Scale bar, 10 μm .

cambrian microfossils have been described in China, they are mainly acritarcha fossils macerated from non-chert rock samples; few microfossils from cherts of both stromatolitic and non-stromatolitic types have been described¹⁰. The assemblages described here are apparently the best Sinian assemblages from south-west China reported to date. (2) The Sinian assemblages occur near the Cambrian/Precambrian boundary, and the abundance of the wider filaments and some stratigraphically definite taxa, such as the *Obruchevella parva* reported only from sediments near the Upper Proterozoic/Lower Phanerozoic boundary⁸, may allow assignment of a late Proterozoic age for the sediments. (3) Although the small and ensheathed colonial unicells and filamentous fossils dominate in the described formations and suggest cyanophytic affinity with Chroococaceae, Oscillatoriaceae and Nostocaceae, the large coccoids are larger than most of the cyanophytic taxa and may be eukaryotic like the members of Chlorophyceae or Rhodophyceae discovered in stromatolitic cherts. This suggests that the stromatolite-building algae are taxonomically similar to the dominant benthic algae inhabiting the supra-, sub- and intertidal late Precambrian environment, and it is of interest to know where and how these microorganisms build the stromatolites. (4) The better preservation of the mineralized microfossils in cherts of the Meishucun Formation in the Meishucun section may indicate the importance of secondary mineralization as a means of preservation and that this kind of microfossil is probably filled by collophanite before replacement by apatite.

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Tree remains in a North York Moors peat profile

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It has been postulated^{1,2} that in the southern Pennines above 350–400 m, burning of the vegetation during Mesolithic time prevented the growth of trees, and that this continued during Neolithic time, although it was suggested that some recolonization of forest took place when agriculture made it possible to diminish the impact of hunters on wild animal food resources and on these uplands. Here we present analogous evidence but come to a slightly different conclusion which may be due to regional differences in prehistoric settlement. Peat profiles such as we describe here are uncommon in the region and so the phenomena may have been spatially restricted.

Table 1 Stratigraphical units at Bonfield Gill Head

Unit letter*	Horizons occupied (cm)	Peat type	Wood and macroscopic charcoal contents*
1	0–20	<i>Sphagnum</i> peat	No charcoal
k	20–40	Well humified peat with some remains of <i>Eriophorum</i>	No charcoal above 41 cm, <i>Betula</i> stump at 38–41 cm
j	40–52 (<i>Ulmus</i> decline at 41 cm)	Less well humified <i>Eriophorum</i> peat, some Ericaceae twigs	
i	52–54	Wood layer and amorphous peat	<i>Betula</i> wood: bark, branches and twigs
h	54–58	Charcoal and amorphous peat	Large pieces of charcoal
g	58–70	<i>Eriophorum</i> peat	
f	70–77	Well humified peat and wood	Small wood pieces (up to 10 × 5 cm)
e	77–81	Peat and charcoal	Charcoal mostly macroscopic but 'soot' also present
d	81–90	Wood fragments and peat	<i>Betula</i> fragments
c	90–97	Minero-organic amorphous peat	
b	97–105	Sand + wood and bark fragments	Tiny pieces of woody material
a	105 →	White clay	

See Fig. 1.

* For 'soot' see Fig. 2.

We examined the peat profile from the head of Bonfield Gill (grid ref. SE 598958: 346m altitude) which runs east-west across Bilsdale Moor in an area of patchy blanket peat which has eroded in places to reveal stumps and trunks of sub-fossil trees (*Betula* and *Quercus* spp.) of a substantial size; the remnants of forest rather than scrub are suggested by trunks 0.6–1.0 m in diameter with roots spreading a further 1.25 m to each side. Investigation of the basal 100 cm of a typical profile of 2-m depth of organic material reveals several stratigraphical units (Table 1 and Fig. 1). The key elements in the stratigraphy are the presence of wood in several layers and the occurrence of charcoal and 'soot' (microscopic charcoal fragments) particles throughout. An estimate of the frequency of the microscopic particles at different horizons is given in Fig. 2. Macroscopic charcoal occurrence is indicated in Table 1. At 38–41 cm there is the base of a well preserved *Betula* tree stump whose remains and attitude leave no doubt that it is *in situ*, together with wood fragments of *Quercus* sp. Above the stump we find fibrous monocotyledonous peats and *Sphagnum* peat typical of blanket mires in upland Britain. This stratigraphy accords with the southern Pennine profiles in recording tree growth after a period of peat accumulation. In the lower peats (52–54 cm, 70–77 cm) the wood remains comprise fragments of birch bark and birch twigs, some of which are so large that they cannot have travelled far, and may represent *in situ* woodland.

Results from the pollen analysis of the basal 100 cm of the profile are displayed as Fig. 1, pollen frequencies being expressed as percentages of total land pollen. The strata described in the stratigraphic column are explained in Table 1, and above this sampled section lay a further metre of humified *Sphagnum* peat. In Fig. 1 certain taxa have been assembled into groups in accordance with their ecological affinities. 'Quercetum Mixtum' includes *Quercus*, *Ulmus* and *Tilia*. 'Heliophyte Shrubs' incorporates light-demanding woody taxa which respond favourably to forest canopy opening; *Prunus*, *Sorbus*, *Salix* and *Fraxinus*. 'Ruderals' includes herbs considered to be colonizers of waste or freshly cleared ground. Zonation of the pollen diagram is by a scheme of local forest clearance stages (FCS) of which three types are defined. Interference (I) phases recording

low-intensity earlier clearance, clearance (C) phases recording higher-intensity later clearance and regeneration (R) phases during which forest clearance is considered not to be taking place. Radiocarbon dates are given in Table 2 and Fig. 1.

Correlation of the pollen and stratigraphical data reveals several interesting features. First, the relationship of the tree stump to a decline of *Ulmus* pollen: the other pollen frequencies, the ^{14}C date and comparison with other North York Moors pollen profiles suggest strongly that this is the *Ulmus* decline of western Europe, usually dated in this region to $\sim 4,750$ yr b.p. (ref. 3). If we accept this marker horizon and agree also that it is the spoor of the incursion of people of Neolithic culture, then the tree stump marks the end of Mesolithic time. Inspection of the pollen frequency curves for the 40–100 cm section of the profile reveals evidence corroborative of the interference with the vegetation suggested, particularly by the charcoal, in Table 1. This evidence takes the form of 'interference phases' of which three are recognized (I1, I2 and I3 on Fig. 1) and two of which are ^{14}C dated to the 5th millennium b.p.

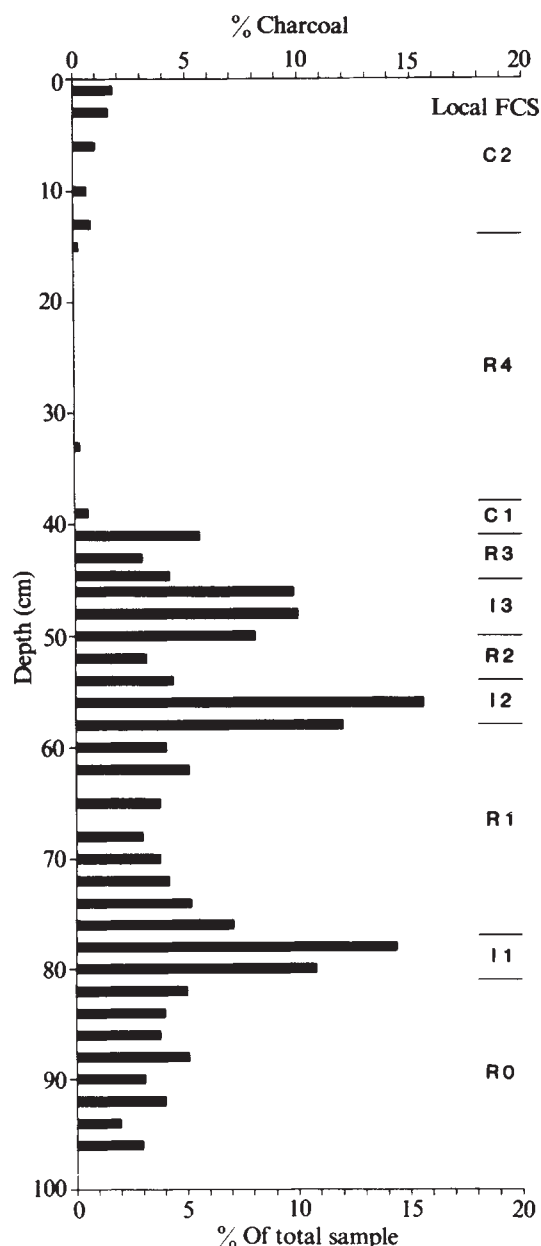


Fig. 1 Selective pollen diagram from Bonfield Gill Head, percentages of total land pollen. The stratigraphical units are identified and described in Table 1 and the FCS zones in the text (R, regeneration; I, interference; C, clearance).

Table 2 Preliminary results of radiocarbon determinations

Sample	No.	Radiocarbon age (yr b.p.)
I1	HAR-4225	5,670 $\pm$ 90
I2	HAR-4226	5,170 $\pm$ 90
I3	HAR-4230	4,610 $\pm$ 80
R4	HAR-4229	4,890 $\pm$ 80

We consider HAR-4230 to be anomalous and have ignored it in the discussion.

In the basal phase R0, *Pinus sylvestris* values are considerable, a feature common to early Flandrian II pollen spectra from the uplands of this region. Non-tree pollen values are also high, with *Corylus*, *Salix* and Gramineae prominent, as well as *Pteridium* spores. The subsequent pollen record implies that the open nature of the vegetation at this stage may be the legacy of an earlier episode of forest clearance, before the inception of peat formation at this site. From a peak at the base of the zone, non-tree pollen values decrease steadily as woodland regeneration continues. This trend towards more wooded conditions is abruptly reversed, however, during phase I1 ($\sim 5,670$ yr b.p.), which marks the virtual demise of *Pinus sylvestris* but sees distinct increases in *Betula* and *Alnus*, with a sharp but temporary peak in the declining *Corylus* curve, echoed in the *Pteridium* spores. *Fraxinus* is recorded for the first time. Some ruderal pollen, including *Melampyrum*, *Rumex*, Cruciferae and Chenopodiaceae, show a first presence, or enhanced frequencies, as does a rather undifferentiated group like Rosaceae which may contain shrubs of open habitat. We interpret this interference phase as the result of forest recession associated with human activity⁴. Phase I1 is succeeded by a regeneration phase (R1) characterized, for example, by higher *Quercus* very high *Betula*, high *Ulmus* and *Tilia* levels, while *Corylus* and *Fraxinus* diminish, the latter to virtually nothing. With the exception of one horizon, *Pteridium* falls off in this phase as do ruderal pollen. Another I phase (I2, $\sim 5,170$ b.p.) follows at 55–58 cm, and then a short regeneration phase (R2) coinciding with a wood layer in the stratigraphy. The phases I2 and I3 are marked by especially high values for 'soot' and the fragments are sub-angular rather than rounded in shape, so that they may not have travelled far. Taxa like *Corylus*, *Pteridium* and heliophyte types *Salix* and *Fraxinus* all increase their frequencies in phase I2, while *Melampyrum*, *Cirsium* and *Rumex* are prominent among the ruderal herbs. Phase I3 (45–51 cm) records very abundant *Pteridium* and a large increase in the type and frequency of ruderal herbs, especially *Melampyrum*, *Artemisia* and *Rumex*, as well as frequencies for *Calluna*, which here exceed 100% of aggregate phase for the first time. This is presumably evidence for either a drier peat surface in the neighbourhood, or for the acidification of mineral soils, as it persists into regeneration phase R3. During the succeeding phase we detect the evidence of forest opening once again in the presence of *Plantago lanceolata* for the first time, along with high frequencies of *Pteridium*, *Melampyrum* and *Betula*. The pollen runs show that this phenomenon has a different character to the I phases and we have called it C1 (clearance 1). It is short lived and another R phase (R4) supervenes, to be interrupted by phase C2 near the top of the pollen diagram at a level where the sampling interval does not permit its detailed discussion. The large *Betula* tree stump in the profile ($\sim 4,890$ yr b.p.) corresponds with phase C1 and the beginning of phase R4.

If the *Ulmus* decline marks the beginning of Neolithic economies in this region, then we should expect phases I1, I2 and I3 to result from Mesolithic man's activity. We infer that they result from the burning of the woodland vegetation at or near the site as charcoal in the I phase is often quite large (15 $\times$ 9 mm pieces are found, for example). The 'soot' in the R phases probably came from burning in the region but far enough away to provide only background 'noise'. Even though doubts

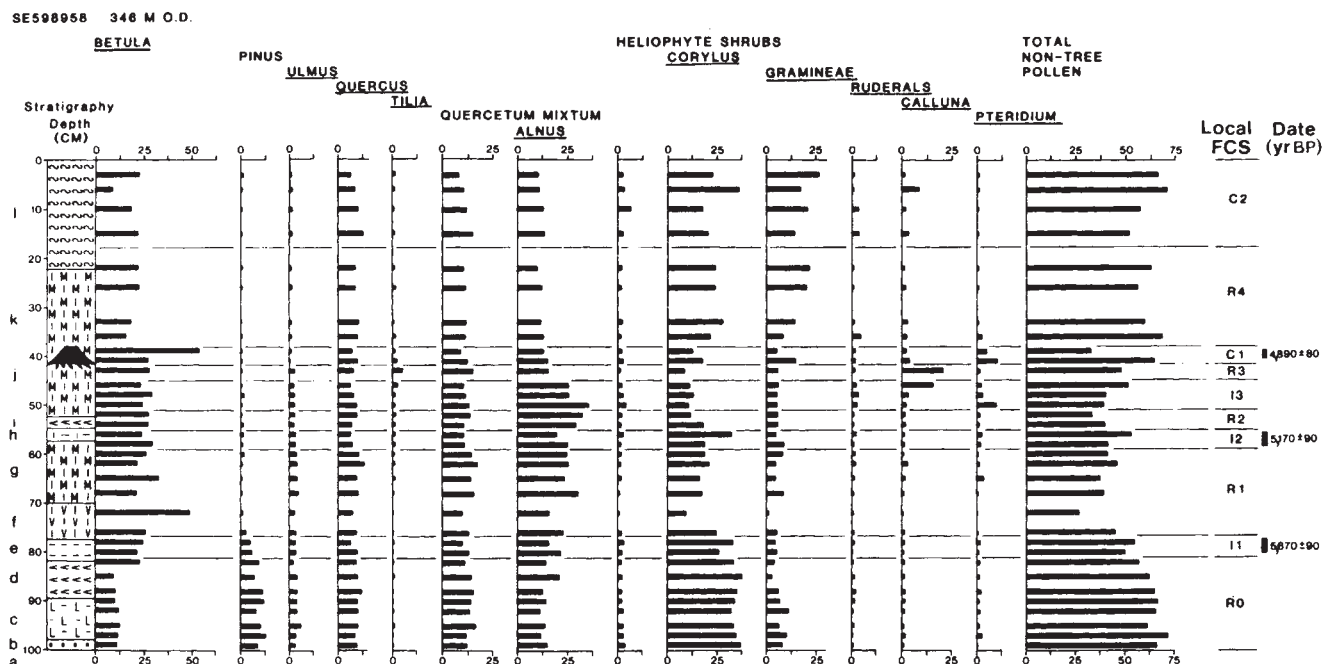


Fig. 2 Charcoal amounts at Bonfield Gill. The quantity of charcoal was estimated from disaggregated peat mixed with water which was spread over a gridded Petri dish. At $\times 60$, the percentage of each square ($\Sigma = 100$) occupied by charcoal and carbonized material was estimated. J.B.I. estimates replicability to within $\pm 3\%$. Note the correspondence with the I-phases identified from the pollen diagram (Fig. 1) and the lack of charcoal in R4: the post *Ulmus* decline phase on the pollen diagram.

have been expressed⁵ on the interpretation of pollen diagrams in archaeological contexts, we believe that we have good evidence of repeated burning of the same site. The I-phase to I-phase interval is, however, longer than theory would predict² and more work is needed to see whether we are dealing with a real interval or whether we can improve the resolution of the technique: is R1 an aggregate phase, for example? Cessation of burning about the time of the *Ulmus* decline seems to have allowed tree growth and phases R1 and R2 could show smaller-scale evidence of the same feature. Even if the burning-recession sequence did not happen exactly here, it must have occurred in the near vicinity.

Finally, we caution that examination of many peat profiles from the North York Moors suggests that the Bonfield Gill site is unusual in its repetitive sequence, and that it is more common for wood to occur at the base of the blanket peat rather than above a sequence of peats and small wood fragments. While it may be that evidence of repeated burning, rather than the phenomenon itself, is patchy, it seems prudent to regard this practice as having had a limited spatial distribution. We emphasize, however, that the Bilsdale Moor area is said to have the highest density of Mesolithic flint sites in the country: this may be relevant circumstantial evidence. We suggest that here the burning seems to have stopped at the beginning of the Neolithic rather than later, as suggested for the southern Pennines; regional differences in occupation of the land by agricultural people could easily account for this point⁶.

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Successful biological control of the floating weed salvinia

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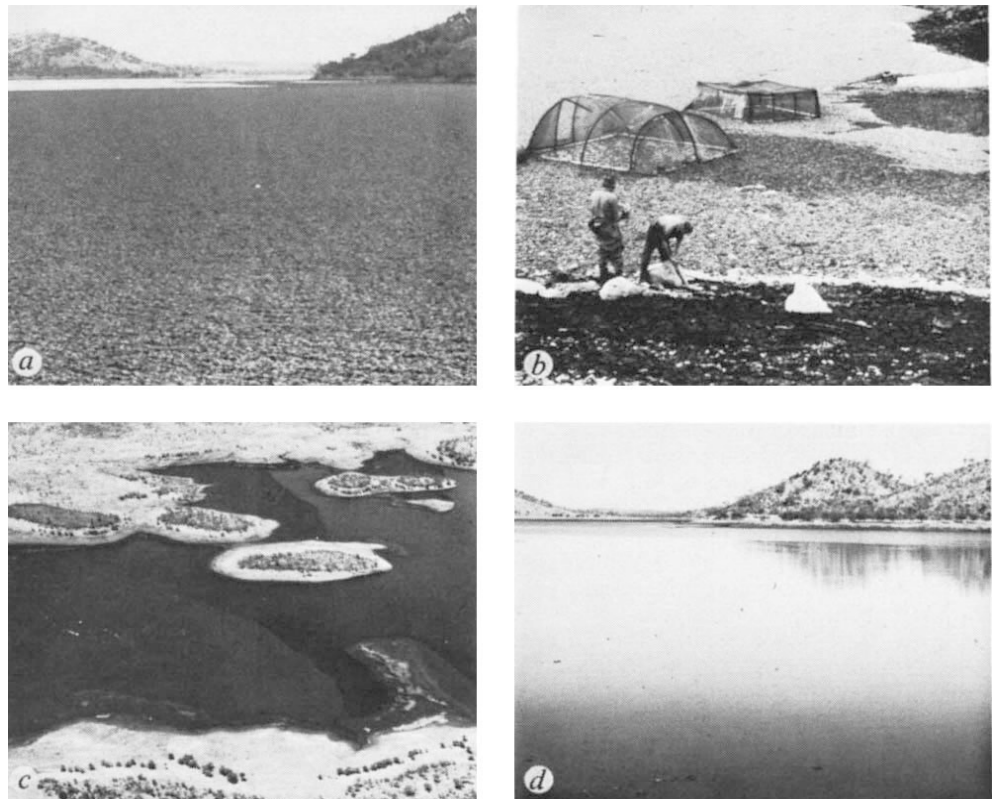
The floating fern *Salvinia molesta* D. S. Mitchell (Salviniaceae) originated in southeastern Brazil¹, but since about 1930, it has been introduced into various tropical and subtropical regions where it has become as great a menace as the water hyacinth²⁻⁴. Biological control of salvinia has clear economic and environmental advantages over other methods of control, but earlier attempts either failed or achieved inconclusive results⁵⁻⁷. We report here successful control of the largest salvinia infestation in Australia using the beetle *Cyrtobagous singularis* Hustache (Curculionidae) and suggest why this beetle has potential for controlling salvinia infestations elsewhere.

Salvinia was first recorded in Australia in 1952 and by 1976 it was present in many tropical and subtropical rivers and lakes and was more widespread than water hyacinth, which entered the country in the late 1800s⁸. Salvinia has achieved unacceptable population densities in Australia and elsewhere due to a combination of extremely high rate of growth, its dry weight doubling in 2.5 days in optimum conditions and an absence of suppressant parasites and pathogens⁸. By 1978 the largest infestation in Australia was on Lake Moondarra near Mt Isa, northern Queensland (20°36' S, 139°32' E), consisting of ~50,000 tonnes fresh weight covering some 400 hectares (Fig. 1a). Attempts to control this infestation using herbicides

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Fig. 1 *S. molesta* on Lake Moondarra in northern Queensland. *a*, In 1978. *b*, Weed damaged by *C. singularis* showed as dark patches on 20 January 1981, nearly 8 months after the beetles were released in and near the cages. *c*, The salvinia, forming a large mat to the left of the picture and smaller mats to the right of promontories, was under heavy attack by *C. singularis* and was uniformly dark brown on 17 May 1981. *d*, Most of the salvinia had been destroyed by 26 May 1981 (compare with *a*).



were abandoned in 1979 after expenditure of A\$160,000 (ref. 9).

The native range of *S. molesta* was unknown until 1978¹ and attempts at biological control until that time, in Africa, India, Sri Lanka and Fiji by the Commonwealth Institute of Biological Control, used insects found attacking the related *Salvinia auriculata* Aublet in northern South America and Trinidad^{5,7}. In 1978, CSIRO Australia started a search for biological control agents in the newly discovered native range of *S. molesta* in southeastern Brazil. No new natural enemies were found, but local races of the three species of insect found by Bennett⁵ to have potential for control were selected: *C. singularis*; the moth *Samea multiplicalis* (Guenée) (Pyrilidae) which was released in northern Queensland in January 1981; and the grasshopper *Paulinia acuminata* (De Geer) (Pauliniidae) whose host specificity is being tested in quarantine in Australia.

Adult *C. singularis* are black, long-snouted weevils, about 2 mm long, which feed on salvinia buds. Eggs are laid among the submerged salvinia roots and larvae graze externally on roots before boring inside the rhizome.

Preliminary studies made in Brazil of *C. singularis* collected from *S. molesta* failed to detect any parasites or pathogens attacking the beetles, and to show whether the beetle could survive on plant species other than *S. molesta*. Eight hundred adults originally from Santa Catarina, Brazil, were then shipped to quarantine in Brisbane, Australia, where more detailed studies confirmed the absence of parasites and pathogens and the host specificity of *C. singularis*. Mass breeding was then started to obtain sufficient numbers for field releases.

On 3 June 1980 about 1,500 adults were released onto a salvinia-covered inlet on Lake Moondarra. About 500 beetles were introduced into each of two cages and the remaining 500 beetles were released immediately outside the cages. By late December, beetle activity had reduced salvinia cover by ~80% in the cages and caused discoloration of plants outside the cages. On 30 December fresh salvinia was added to the cages and the doors were left open.

Figure 1*b* shows the cages and the mouth of the inlet on 20 January 1981. The pale salvinia at the top left is healthy. A patch

of pale salvinia was blown around the square cage by strong winds the previous day and is nearly surrounded by darker salvinia damaged by *C. singularis*. Figure 2 shows the distributions of adult beetles and damage along a transect from the pale salvinia through the darker salvinia and further up the inlet. There was clearly a good correlation between the visual impression of damage from a distance and the proportions of leaves and buds damaged. It was also clear that beetles were moving away from heavily damaged salvinia, both onto newly available

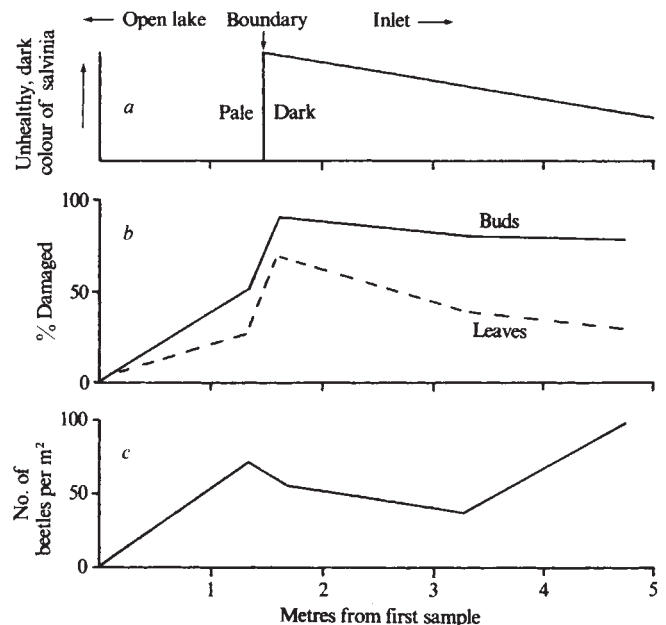


Fig. 2 Transect through the invasion front shown in Fig. 1*b*. *a*, Represents the sharp boundary between pale, healthy salvinia on the left and darker, unhealthy plants. *b* Shows the percentages of buds and leaves damaged by *C. singularis* and *c* shows the numbers of adult *C. singularis* per m² at five points along the transect.

undamaged plants and further up the inlet away from the population focus. No beetles or damage were found elsewhere on Lake Moondarra at this time.

On 20 January 1,500 more beetles were released onto salvinia about 300 m from the inlet and 10 large bags of beetle-infested salvinia were moved to the opposite side of the lake. A violent storm in February swept most of the remaining beetle-infested salvinia out of the inlet into the main body of the lake.

In late March salvinia throughout the lake started to turn brown and become waterlogged. On 18 April, all the salvinia was dark brown and samples taken at two sites 2 km apart contained respectively 60 and 80 adult *C. singularis* per m², suggesting a total population of >100 million beetles. Population sizes of eggs, larvae and pupae were not estimated. Ninety-nine per cent of buds in both samples had been damaged. Damage was remarkably evenly distributed (Fig. 1c), suggesting an effective mode of beetle dispersal. A blacklight operated on the shore of the lake for 1 h from dusk was found to attract large numbers of strongly flying *C. singularis*.

By 26 May there was very little salvinia left (Fig. 1d). Three samples collected more than 1 km apart contained 100, 70 and 90 adult *C. singularis* per m², which suggests a total population of about 6 million beetles. Ninety-nine per cent of the buds in each sample had been damaged.

Figure 3 presents estimates of the area and fresh weight of salvinia from August 1979 to 26 May 1981. The quantity of salvinia peaked in the autumn of each year until 1981. Drought starting early in 1978 reduced the autumn peak from 50,000 tonnes in 1978 to 19,000 tonnes in 1980 as the lake contracted in area to about 50% of maximum and salvinia was stranded. Substantial rain in January and February 1981 increased the area of the lake to ~80% of maximum and was expected to result in an autumn peak of 30,000 to 40,000 tonnes of salvinia. Some increase occurred to February 1981, after which *C. singularis* destroyed ~8,000 tonnes in 3 months and prevented significant regrowth. By August 1981 there was estimated to be <1 tonne of salvinia left. Despite the large quantity of salvinia killed and sunk, no algal blooms or other deleterious changes in water quality were detected (A. McCredie, personal communication). Based on analogous cases of biological control agents causing sudden collapses of dense populations of weeds¹⁰, we expect salvinia and *C. singularis* will be able to coexist on Lake Moondarra in a dynamic equilibrium at low population densities. However, both weed and control agent may become extinct on the lake if the remaining salvinia becomes stranded and dehydrated before the advent of the wet season in December 1981.

Why has *C. singularis* been so successful on Lake Moondarra, and has it the potential to control salvinia elsewhere? Attempts to establish the species on salvinia in Botswana and Zimbabwe in

the early 1970s failed⁵, as did attempts to breed it in Fiji⁷. In these cases the beetles used were collected from *S. auriculata* in Trinidad, whereas the plant on which establishment was attempted was *S. molesta*. Although taxonomists recognize beetles collected from both species of plant as *C. singularis*, the Australian success may be due to our having obtained a race particularly adapted to *S. molesta*. If this is the case, we may have solved the intractable problems caused by *S. molesta* in Africa^{2,11}, India^{2,4}, Sri Lanka², Indonesia², Papua New Guinea³, New Zealand and Fiji⁷, and elsewhere in Australia.

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Enkephalin as a transmitter for presynaptic inhibition in sympathetic ganglia

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The endogenous opioid peptides, enkephalins, are known to be concentrated in discrete populations of central and peripheral neurones^{1–3} and to inhibit synaptic transmission through a presynaptic mechanism reducing the release of transmitters^{4–6}. These observations led to a hypothesis that enkephalin may serve as a transmitter for presynaptic inhibition at central and peripheral synapses^{4,5}. To substantiate this hypothesis it is of crucial importance to demonstrate at specified synapses an inhibitory process that is evoked by stimulation of enkephalin-containing nerve fibres and is blocked by the opiate antagonist, naloxone. Mammalian sympathetic ganglia may provide a useful model for exploring this possibility, because enkephalin was shown, using immunohistochemistry³, to exist in certain nerve terminals in the ganglia and to inhibit cholinergic and noncholinergic transmission by a presynaptic mechanism^{5,7,8}. We now report that in mammalian prevertebral ganglia, the conditioning stimulation given to preganglionic nerves produces a long-lasting presynaptic inhibition of cholinergic transmission and that this inhibition is specifically abolished by naloxone. The results strongly suggest that enkephalin or closely related peptide(s) liberated from certain preganglionic fibres act as a transmitter for presynaptic inhibition, regulating the release of acetylcholine (ACh) in the sympathetic ganglia.

Experiments were carried out on the inferior mesenteric ganglia isolated from adult guinea pigs. The ganglion was placed in a bath and perfused with modified Tyrode solution at 36 °C. Intracellular recordings were made from ganglion cells as described previously^{5,8}. Test stimuli were given to a small bundle of the lumbar splanchnic nerve through a suction electrode to evoke cholinergic fast excitatory postsynaptic potentials (e.p.s.ps). To the remaining preganglionic nerves, that is, the lumbar splanchnic and/or intermesenteric nerves,

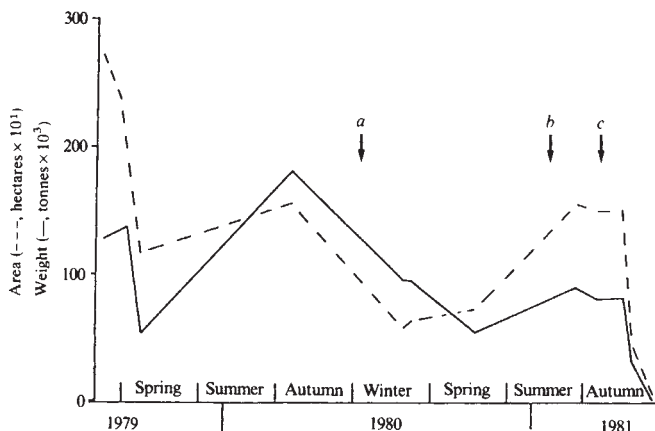


Fig. 3 Fluctuations in the area (---) and fresh weight (—) of salvinia on Lake Moondarra. a, First release of *C. singularis*; b, significant rainfall and second release + redistribution of beetle-infested plants; c, first appearance of widespread damage to salvinia. (Data courtesy of Mount Isa Mines Ltd.)

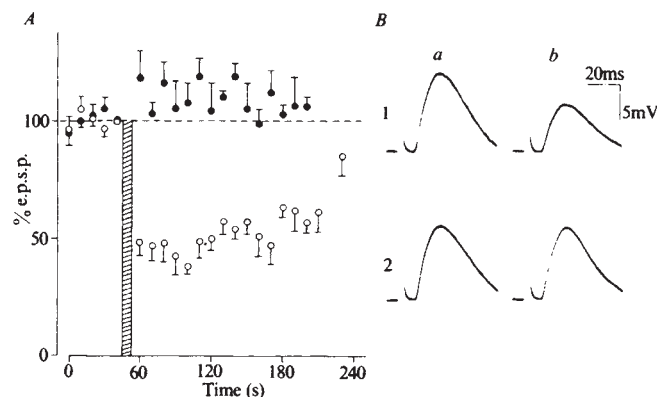


Fig. 1 Inhibitory effect of conditioning stimulation on cholinergic e.p.s.ps recorded from neurones in the inferior mesenteric ganglia, and antagonism by naloxone. Test e.p.s.ps were evoked by stimulating a small bundle of the lumbar splanchnic nerve at 1 Hz. Conditioning stimulation at 50 Hz for 8 s was given to the remaining lumbar splanchnic nerves during the period shown by the hatched column in A. A, eight successive e.p.s.ps were averaged every 10 s and recorded (see sample records in B). The amplitude of each averaged e.p.s.p. was expressed as a percentage of the control that was recorded immediately before the conditioning stimulation. Each point and vertical bar represent the mean $\pm$ s.e.m. obtained from three successive observations repeated at 6-min intervals on the same neurone. $\circ$, In control solution; and $\bullet$, in the solution containing naloxone ($3 \mu\text{M}$). B, sample records of the averaged e.p.s.ps in another experiment. a, Test responses during the control periods; and b, conditioned responses obtained during the 15–20 s after the end of conditioning stimulation (50 Hz for 8 s). 1, In control solution; and 2, in the presence of naloxone ($3 \mu\text{M}$).

conditioning stimulation was given with one or two separate suction electrodes.

Since the enkephalin-containing nerve terminals in the prevertebral sympathetic ganglia are thought to originate mainly from the preganglionic fibres^{3,9}, we sought to establish whether stimulation of preganglionic nerves produces an inhibitory effect on the cholinergic fast e.p.s.ps. After conditioning stimulation (50 Hz for 8 s), the amplitude of signal-averaged test e.p.s.ps was reduced to <50% of the averaged size of control e.p.s.ps, and the inhibition lasted for 2–4 min (Fig. 1). Such a prolonged inhibitory effect became obvious with the conditioning stimulation at 50 Hz for 2 s, and its magnitude depended on the number of conditioning stimuli. The maximal extent and the half-decay time of the inhibition produced by the preganglionic stimulation (50 Hz for 8 s) were $70.5 \pm 4.7\%$ and 56.4 ± 5.8 s respectively (mean $\pm$ s.e.m. in 12 cells).

The inhibitory effect of the conditioning preganglionic stimulation on cholinergic e.p.s.ps was abolished by addition of naloxone ($1\text{--}3 \mu\text{M}$) (Fig. 1). Naloxone in the same concentration range almost completely blocked the inhibitory action of a potent enkephalin analogue, [D-Ala²]-Met-enkephalinamide ($0.3\text{--}2 \mu\text{M}$), on cholinergic e.p.s.ps⁷. To test the specificity of the action of naloxone, we examined its effects on the inhibition produced by other substances. Noradrenaline ($10\text{--}50 \mu\text{M}$), dopamine ($20\text{--}100 \mu\text{M}$) and γ -aminobutyric acid ($20\text{--}50 \mu\text{M}$) depressed the cholinergic e.p.s.ps in the sympathetic ganglia^{10–12}, but the inhibitory effects of these substances were not affected by naloxone ($3 \mu\text{M}$). An α -adrenergic blocker, phentolamine ($1.5\text{--}3 \mu\text{M}$), on the other hand, abolished the effect of noradrenaline, but did not affect the neurally evoked inhibition of cholinergic fast e.p.s.ps. Furthermore, this inhibition remained unchanged in the presence of atropine ($2 \mu\text{M}$). Therefore, it is unlikely that catecholamine-containing interneurons are involved in this inhibitory process¹³.

Further experiments were carried out to determine whether the mechanism of this inhibition is pre- or postsynaptic. The sensitivity of the postsynaptic membrane to ACh and the input resistance of ganglion cells were determined before and after conditioning stimulation. In the experiment shown in Fig. 2,

both the sensitivity to ACh and the membrane resistance of a ganglion cell increased slightly 10–60 s after the end of conditioning preganglionic stimulation (50 Hz for 8 s). In contrast, during the same period, the mean size of e.p.s.ps recorded from the same neurone was reduced to 15–60% of the control (Fig. 2a). The slight increase in the ACh-induced depolarization as well as in the membrane resistance may be due to the noncholinergic slow e.p.s.p. produced by preganglionic stimulation⁷. These results can be explained by the hypothesis that the neurally evoked inhibition is caused mainly by a presynaptic mechanism reducing the amount of ACh release.

This hypothesis was further supported by quantal analysis of the e.p.s.ps during the control and conditioned periods (Fig. 3). On an assumption that the quantal release of ACh can be predicted by Poisson statistics^{14,15}, the mean number of ACh quanta released by each test stimulus was estimated from the number of failures in a series of trials. During the period 10–170 s after conditioning stimulation (50 Hz for 12 s), the number of failures showed a ninefold increase over that observed during the control period (stippled columns in Fig. 3; see also Fig. 2a) and the mean quantum content of the e.p.s.ps was reduced to about 40% of the control. In contrast, the estimated size of the quantal unit did not change significantly after the conditioning stimulation (arrows in Fig. 3). Essentially the same results were obtained in eight other experiments, where the conditioning preganglionic stimulation (50 Hz for 8–12 s) reduced the mean quantum content to $54.7 \pm 3.5\%$ of the control (mean $\pm$ s.e.m.) while the unit size of e.p.s.ps during the conditioned period was $107.7 \pm 5.2\%$ of the control. The results, therefore, support the presynaptic nature of this neurally evoked inhibition. The effects of conditioning stimulation in increasing the number of failures and reducing the quantum content of e.p.s.ps were also reversed by naloxone (Fig. 3c). Naloxone alone, however, did not significantly affect the unit size or mean size of e.p.s.ps (Fig. 1B).

The present findings, together with other lines of evidence with regard to the action and the presence of enkephalin^{3,5},

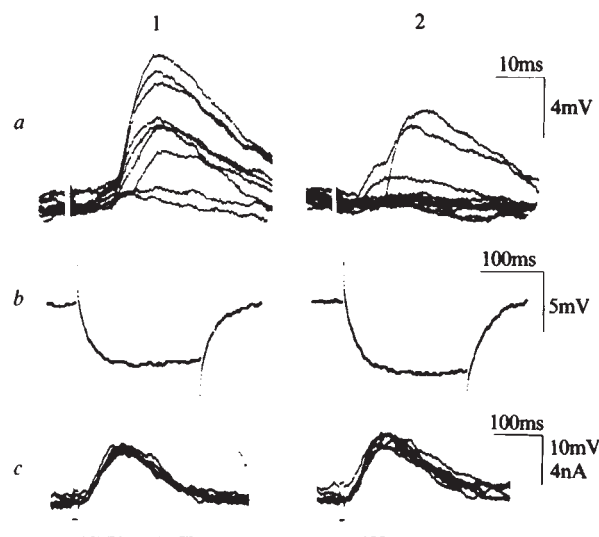


Fig. 2 Effects of conditioning stimulation on cholinergic e.p.s.ps, electrotonic potentials, and ACh-induced depolarizations recorded from a neurone in the inferior mesenteric ganglion. Test and conditioning stimulation were given to the preganglionic nerves in the same way as for Fig. 1. ACh was iontophoretically applied to the neurone with current pulses once every 2 s. a, Test e.p.s.ps evoked at 1 Hz; nine traces were superimposed. b, Averaged electrotonic potentials produced by hyperpolarizing current pulses of 0.1 nA and 200 ms duration injected into the neurone at 1 Hz; eight responses were averaged. c, ACh-induced depolarization (upper traces) and current pulses passed through the ACh-containing electrode (lower traces); five traces were superimposed. 1, Responses recorded during the control period; and 2, responses recorded 20–30 s after the end of conditioning stimulation (50 Hz for 8 s).

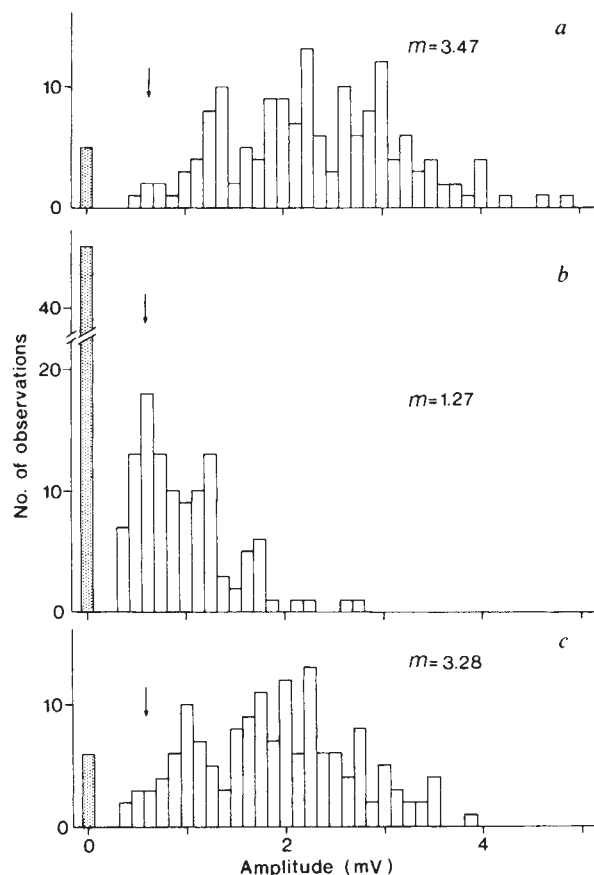


Fig. 3 Amplitude histograms of the control and conditioned cholinergic fast e.p.s.ps recorded from a neurone in the inferior mesenteric ganglion, and the effect of naloxone on the neurally evoked inhibition. Test e.p.s.ps were evoked at 1 Hz in a series of about 350 trials, and the conditioning stimulation (50 Hz for 12 s) was given at the middle of the series. Each histogram was compiled from the test responses in 160 trials. *a*, Amplitude distribution of test responses recorded during the control period before the conditioning stimulation. *b*, *c*, Amplitude distributions of conditioned test responses recorded during the periods 10–170 s after the end of the conditioning stimulation. *a* and *b* were obtained in control solution, and *c* in the solution containing naloxone (3 μ M). The quantum content, m , was estimated from the number of test stimuli ($n = 160$) and that of failures (stippled columns). The estimated unit size of the e.p.s.ps is shown by arrows.

support the hypothesis that the neurally evoked presynaptic inhibition of cholinergic e.p.s.ps in the guinea pig sympathetic ganglia is mediated by enkephalin or closely related peptide(s) released from certain preganglionic fibres. Previous studies suggested that substance P is a transmitter released from the axon collateral terminals of visceral afferent fibres to generate the noncholinergic slow e.p.s.p. in the prevertebral ganglion cells^{7,8} and that enkephalin inhibits presynaptically the noncholinergic slow e.p.s.p.⁷. Thus, the signal transfer processes in the ganglia involve not only the classical cholinergic transmission but also the slow synaptic events mediated probably by peptidergic transmitters such as enkephalin and substance P, which serve to modulate the sympathetic tone regulating the visceral organs. Recent studies showed that naloxone-reversible inhibitory processes may exist in certain areas of the central nervous system^{16,17}. Furthermore, it has been suggested that enkephalin inhibits the substance P-mediated excitation in the spinal trigeminal nucleus by presynaptic mechanism⁴. It is, therefore, likely that enkephalin acts as a transmitter in presynaptic inhibition that controls the release of ACh, substance P and possibly other transmitters in central and peripheral synapses.

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Breakdown of cytoskeletal filaments selectively reduces Na and Ca spikes in cultured mammal neurones

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Cytoskeletal filaments, which contain microtubules^{1–4} (~25 nm thick), microfilaments^{5,6} (5 nm) and intermediate filaments^{7–9} (neurofilaments, 10 nm), are considered essential for maintaining complex cellular shape and various cellular functions. Several studies have claimed that these filaments also maintain in some part physiological properties of excitable membranes^{10–14}. However, the role of these filaments in maintenance of ionic channel activity is poorly understood^{10,11}. Here we report experiments in which we disrupted specific cytoskeletal filaments by applying chemicals to tissue-cultured nerve cells of adult guinea pigs^{15–17}, and examined changes in membrane properties by conventional electrophysiological techniques. Selective breakdown of microfilaments by cytochalasin B^{5,6,18–21} or its derivatives^{22–24} caused selective reduction in the membrane capacity to carry Na ions¹⁶ (as measured by V_{max} of pure Na spikes). The ability of the membrane to carry Ca ions¹⁵ and other physiological properties (resting membrane potential, input resistance and capacitance) were not affected significantly. By contrast, a breakdown of microtubules by colchicine^{1–4} or vinca alkaloids^{4,25} caused selective reduction of V_{max} for Ca spikes but not of that for Na spikes. These findings suggest that Na channels in the plasma membrane may have a molecular interaction with microfilaments, but are independent of microtubules. Conversely, Ca channels may be related to microtubules or to neurites, but seem to be independent of microfilaments.

The techniques used in tissue culture of nerve cells from adult guinea pigs have been reported elsewhere^{15–17}. Dorsal root ganglia were incubated with collagenase in L-15 medium, and nerve cells isolated from the ganglia by vibration. The nerve cells were grown in collagen-coated plastic dishes on growth medium (75% Eagle's medium, 15% fetal calf serum, 9% chick embryo extract and 1% penicillin-streptomycin solution) in air containing 5% CO₂ at 37 °C.

After 2 days of culture, cytochalasin B and colchicine, prepared as described below, were added to the tissue culture dishes (1.5 ml growth medium per dish) using a microsyringe. At this stage of culture, nerve cells were starting to extend their neurites^{15,17} (Fig. 1a). Cytochalasin B (1 mg) was first dissolved in dimethyl sulphoxide (DMSO, 1 ml), then diluted with L-15 medium to give a final concentration in stock solution of

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Table 1 Changes in resting membrane properties and Na spike component of cultured nerve cells after exposure to cytochalasin B and colchicine

		Resting membrane potential (mV)	Input resistance (M Ω)	Input capacitance (pF)	$V_{\max}$ of Na spikes (V s $^{-1}$)	Ratio
Cytochalasin B	(4 μ g ml $^{-1}$, 2 days)	-50 $\pm$ 11 (n = 19)	35 $\pm$ 13	45 $\pm$ 15	76 $\pm$ 22 (n = 16)	
Control	(DMSO)	-51 $\pm$ 9 (15)	34 $\pm$ 10	41 $\pm$ 16	113 $\pm$ 31 (15)	0.67*
Cytochalasin B	(6 μ g ml $^{-1}$, 2 days)	-55 $\pm$ 10 (15)	42 $\pm$ 18	56 $\pm$ 18	89 $\pm$ 18 (13)	
Control	(L-15)	-54 $\pm$ 15 (7)	38 $\pm$ 12	50 $\pm$ 15	128 $\pm$ 18 (6)	0.70*
Cytochalasin B	(12 μ g ml $^{-1}$, 1 day)	-48 $\pm$ 6 (7)	36 $\pm$ 10	49 $\pm$ 15	34 $\pm$ 11 (6)	
Control	(L-15)	-50 $\pm$ 6 (7)	33 $\pm$ 9	52 $\pm$ 19	121 $\pm$ 25 (5)	0.28†
Colchicine	(8 μ g ml $^{-1}$, 2 days)	-50 $\pm$ 8 (20)	35 $\pm$ 11	46 $\pm$ 16	100 $\pm$ 34 (17)	
Control	(L-15)	-52 $\pm$ 9 (17)	32 $\pm$ 14	53 $\pm$ 18	118 $\pm$ 55 (15)	0.85
Colchicine	(16 μ g ml $^{-1}$, 2 days)	-45 $\pm$ 7 (18)	30 $\pm$ 5	43 $\pm$ 17	108 $\pm$ 36 (16)	
Control	(Lumicolchicine)	-47 $\pm$ 8 (21)	32 $\pm$ 19	45 $\pm$ 18	110 $\pm$ 32 (14)	0.98
Colchicine	(20 μ g ml $^{-1}$, 1 day)	-54 $\pm$ 7 (15)	29 $\pm$ 10	77 $\pm$ 30	154 $\pm$ 32 (11)	
Control	(L-15)	-52 $\pm$ 8 (12)	31 $\pm$ 12	68 $\pm$ 28	161 $\pm$ 43 (11)	0.96

All values are mean $\pm$ s.d.; numbers of neurones examined are indicated in parentheses. The nerve cells were immersed in a Co $^{2+}$ - and TEA $^{+}$ -containing medium (see Fig. 2 legend), in which the nerve cells generated pure Na spikes. Input resistance and capacitance were obtained by intracellular passage of a small hyperpolarizing pulse current (up to 0.3 nA for 16 ms), assuming that the membrane was a single resistance-capacitance circuit. Pure Na spikes were elicited, as seen in Fig. 2; $V_{\max}$ of the spikes were obtained by electronic differentiation. Before passage of pulse current the membrane potential of the penetrated nerve cells was held at ~ -100 mV, where the current-voltage relationship is approximately linear and the membrane generates a full-sized Na spike. Note that no change was induced in resting membrane properties of the nerve cells after exposure to cytochalasin B and colchicine.

* $P < 0.01$; † $P < 0.001$ (Student's t -test).

100 μ g ml $^{-1}$. Dihydrocytochalasin B 23,24 and cytochalasin D 22 were prepared in the same way. Control solutions consisted of either L-15 medium alone or L-15 medium containing 10% DMSO. Colchicine, vinblastine sulphate, vincristine sulphate and colcemide were stored as solutions (2 μ M) in L-15 medium. Control solutions for these alkaloids were either L-15 medium alone or L-15 medium containing 800 μ g ml $^{-1}$ (2 μ M) lumicolchicine (prepared by UV illumination of colchicine dissolved in 99% ethanol 25).

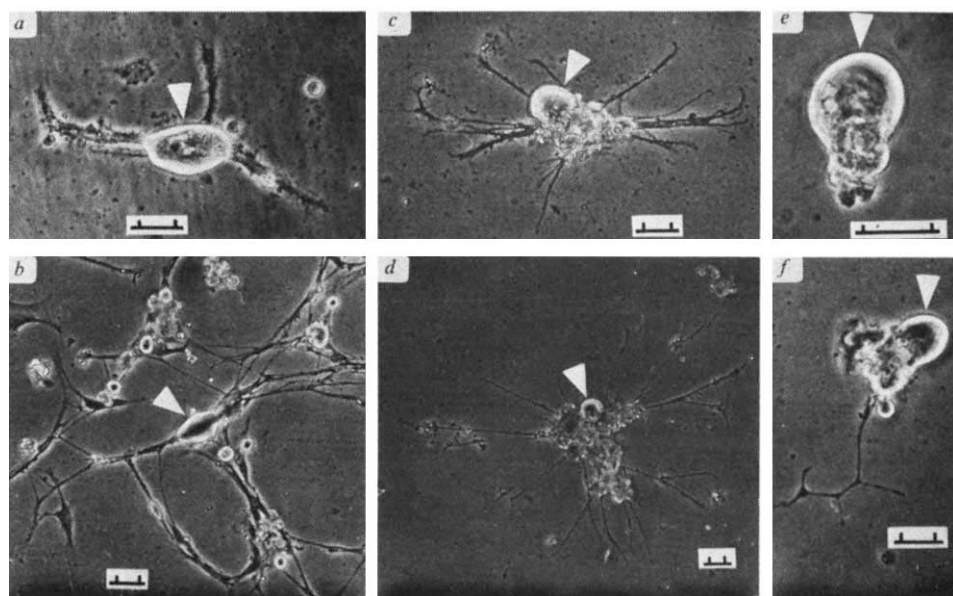
Cultured nerve cells were penetrated by a glass micro-electrode (20–30 M Ω) filled with 3 M KCl. To elicit spikes and measure membrane resistance and capacitance, d.c. and pulse currents (up to 5 nA) were passed intracellularly through the microelectrode. The intracellular potential was determined by a Wheatstone bridge balance. Input resistance and capacitance were measured using a small pulse current while holding the membrane potential at ~ -100 mV; the nerve cell was assumed to be a single RC circuit 16 . Na and Ca spikes were elicited using depolarizing pulses. Pure Na spikes were elicited in nerve cells bathed in a Co $^{2+}$ -containing solution (see ref. 16 and Fig. 2 legend); Co $^{2+}$ was added to inhibit Ca spikes 26 , which otherwise are superimposed on the Na spikes. Pure Ca spikes were elicited in nerve cells bathed in a Na-free tetraethylammonium (TEA)-containing solution (see ref. 15 and Fig. 2 legend). Before spike

initiation, the membrane potential of the penetrated nerve cell was hyperpolarized to a potential more negative than -100 mV. This continuous hyperpolarization eliminated inactivation of Na and Ca channels which occurs at a small resting membrane potential $^{15-17}$ (Table 1). The $V_{\max}$ of a full-sized spike elicited during the hyperpolarization was obtained by electronic differentiation; this $V_{\max}$ was considered proportional to the largest amplitude of inward Na or Ca currents in the membrane 27 , and was compared for nerve cells grown in different conditions.

Cytochalasin B caused several distinct morphological changes in nerve cells (Fig. 1c, d). (1) Growth of neurites was reduced at a low dose (4 μ g ml $^{-1}$) and suppressed at the higher dose of 12 μ g ml $^{-1}$: nerve cells tended to have fine neurites that were relatively short. (2) Neuronal somata became spherical; and (3) within a few days of exposure, the nerve cell population was reduced (2/3 to 1/2) due to loss of nerve cells from the monolayer. (4) Growth of fibroblasts and Schwann cells was inhibited. These changes can be regarded as selective breakdown of microfilaments by cytochalasin B $^{5,6,18-21}$. DMSO alone, added as a control, caused no significant morphological or population change in both neuronal and glial cells (results not shown).

Intracellular recordings of nerve cells exposed to cytochalasin

Fig. 1 Changes in morphology of cultured nerve cells after exposure to cytochalasin B or colchicine. *a*, Nerve cell which, after 2 days in tissue culture, started to extend neurites from the somata (triangle). *b*, Control nerve cell (triangle) after 4 days of culture. *c*, *d*, Neurones after exposure to cytochalasin B. These cells were maintained in culture for 4 days, and exposed to cytochalasin B at a concentration of 12 μ g ml $^{-1}$ (*c*) or 4 μ g ml $^{-1}$ (*d*) during days 2 to 4. Note the sparse neurite growth compared to control cells (*b*). *e*, *f*, Neurones exposed to colchicine (16 μ g ml $^{-1}$) during days 2 to 4 of tissue culture. Most nerve cells became spherical (*e*). Some cells had fine neurites of a very short length (*f*). Calibration bars: 20 μ m.



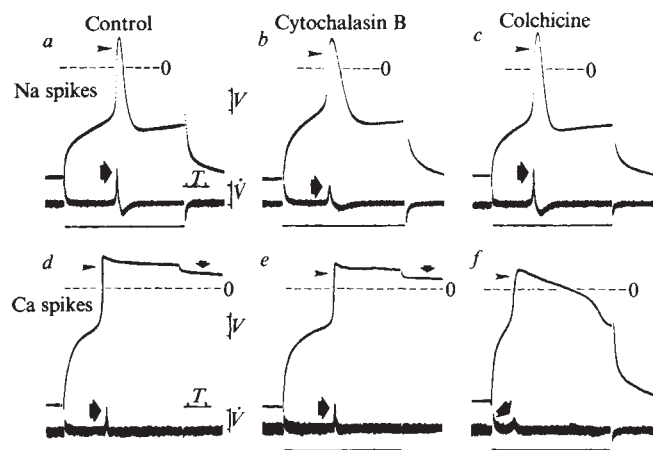


Fig. 2 Na and Ca spikes elicited in cultured nerve cells exposed to cytochalasin B or colchicine. Na spikes (wedges in *a-c*) and Ca spikes (wedges in *d-f*), elicited in normal cells (*a, d*), cytochalasin B-treated cells ($4 \mu\text{g ml}^{-1}$; *b, e*) and colchicine-treated cells ($16 \mu\text{g ml}^{-1}$; *c, f*). All nerve cells were maintained *in vitro* for 4 days, and were exposed to the chemicals during days 2 to 4 of tissue culture. Na spikes were elicited in nerve cells in medium containing 141 mM NaCl, 1 mM CoCl_2 , 1 mM CaCl_2 , 10 mM TEA-Cl, 5.5 mM KCl, 5.5 mM glucose and 2 mM Na-HEPES at pH 7.4. Ca spikes were elicited in Na-free medium containing 80 mM TEA-Cl, 63 mM Tris-HCl, 10 mM CaCl_2 , 5.5 mM KCl and 5.5 mM glucose, pH 7.4. Downward arrows in *d* and *e* show that overshoots of Ca spikes were still present even after cessation of depolarizing pulse-current passage. However, Ca spikes in colchicine-treated nerve cells were of short duration (*f*). Lower traces of *a-f* were obtained by electronic differentiation of the upper intracellular records. $\dot{V}_{\text{max}}$ of the spikes (arrows) were considered to be proportional to transient inward Na or Ca currents associated with the respective spikes. Bars underneath indicate the duration of depolarizing pulse currents passed intracellularly. Calibrations: *T*, 2 ms for *a-c* and 20 ms for *d-f*; *V*, 20 mV for *a-f*; $\dot{V}$, 80 V s^{-1} for *a-c* and 10 V s^{-1} for *d-f*. Further details are given in the text.

B for 1–2 days revealed resting membrane properties (resting potential, input resistance and capacitance, and $I-V$ relationship) that were very similar to those of normal nerve cells (Table 1). The nerve cells were also capable of generating both Na and Ca spikes (Fig. 2*b, e*). The most remarkable effect of cytochalasin B exposure was a selective reduction in $\dot{V}_{\text{max}}$ of the Na spikes (arrow in the lower trace of Fig. 2*b*, and Table 1). This reduction, which was small at 6 h (85% of normal value, $P < 0.2$), became apparent ($P < 0.01$) in 2 days (Table 1). A higher dose of cytochalasin B induced a larger reduction in a shorter period (Table 1). However, this was associated with a great loss of cells. This reduction in the $\dot{V}_{\text{max}}$ of the Na spikes disappeared 2 days after removal of cytochalasin B from the growth medium (data not shown). Similar specific reduction in the Na spikes was induced by dihydrocytochalasin B and cytochalasin D (results not shown) which also cause breakdown of microfilaments^{22–24}. By contrast, there was no change detected in Ca spikes (Fig. 2*e* and Table 1), even when dose and time of exposure to cytochalasin B were increased. These results indicate that the mechanisms required to generate Ca spikes are independent of microfilaments.

Exposure of the cultured nerve cell to colchicine ($16 \mu\text{g ml}^{-1}$) for 2 days caused retrogression of neurites (Fig. 2*c, f*), and produced spherical somata and a reduction in nerve cell population. Colchicine inhibited growth of fibroblasts and Schwann cells on the dishes, which can be explained by a breakdown of microtubules by colchicine^{1,3,4}. Lumicolchicine ($128 \mu\text{g ml}^{-1}$), added as a control, did not change neuronal and glial morphology (results not shown). The most remarkable changes in membrane properties effected by colchicine were a small $\dot{V}_{\text{max}}$ and a short duration of Ca spikes (Fig. 2*f* and Table 2). These changes in the Ca spikes appeared within 1–2 days of colchicine application, but disappeared 3 days after its removal (not

shown). A higher dose of colchicine or a longer period of exposure resulted in only a slightly smaller $\dot{V}_{\text{max}}$ (Table 2). By contrast, no statistically significant change ($P < 0.2$) was observed for Na spikes (Fig. 2*c*, Table 1), resting potential, input resistance and capacitance (Table 1). A similar specific reduction in $\dot{V}_{\text{max}}$ of the Ca spikes was induced by other vinca alkaloids (vinblastine, vincristine and colcemide; data not shown)—these also disrupt microtubules^{1–4,25}.

These experiments demonstrate that, even though cytochalasin B and colchicine induce drastic changes in cell morphology, many nerve cells exhibit healthy electrophysiological properties. In particular, the lack of significant change in input resistance and capacitance (first order approximation) indicates that the basic structure and function of the plasma membrane seem to be maintained. Assuming that capacitance of unit area of the plasma membrane remained unchanged, the small $\dot{V}_{\text{max}}$ of the Na spikes induced by cytochalasin B is considered to be due to a reduction in inward Na currents²⁷, which may be explained further as a reduction in Na channel density in the membrane or as a conformational change in Na channels. Reduction in electromotive force of Na current does not seem to be a main cause because Na spikes in the cytochalasin B-treated nerve cells showed a large overshoot or, for a few cells, only a small reduction in spike amplitude (threshold to peak) of ~ 10 mV. It is highly unlikely that K currents were increased by cytochalasin B because the K conductance should, in part, affect Ca spikes.

The selective reduction in Na spikes by cytochalasin B suggests an interaction between microfilaments and Na channel molecules¹⁰. However, this interaction may not always be simple, as at least 24 h are required to induce an apparent change in the Na spikes. Possible interactions are: (1) microfilaments may constitute major anchoring filaments of Na channel molecules in the plasma membrane; (2) microfilaments may be involved in transportation of Na channel molecules into the plasma membrane; (3) they may contribute to synthesis of Na channels in nerve cells. By contrast, the fact that colchicine had little effect on Na spikes indicates that the Na channels in the membrane may be independent of microtubules¹¹.

The reduced Ca spike caused by colchicine treatment of nerve cells suggests an interaction between microtubules and Ca channel molecules: that is, microtubules may contribute to maintaining Ca channels in the plasma membrane, for example, as an anchoring cytoskeletal filament. However, some observations do not conform to this idea. First, electron-microscopical observations have generally failed to demonstrate microtubules at presynaptic nerve terminals, which are presumed to be rich^{26,28} in Ca channels. In a few studies where microtubules are found in nerve terminals, they seem to be

Table 2 Changes in Ca spike component of cultured nerve cells exposed to cytochalasin B and colchicine

		$\dot{V}_{\text{max}}$ of Ca spikes (V s^{-1})	Ratio
Cytochalasin B	($6 \mu\text{g ml}^{-1}$, 2 days)	4.8 ± 2.5 ($n = 12$)	
	(DMSO)	4.9 ± 1.8 (14)	0.98
Cytochalasin B	($10 \mu\text{g ml}^{-1}$, 3 days)	8.0 ± 2.1 (11)	
	(L-15)	8.7 ± 2.8 (8)	0.92
Colchicine	($16 \mu\text{g ml}^{-1}$, 1 day)	2.7 ± 1.6 (9)	
	(L-15)	4.6 ± 1.2 (12)	0.59*
Colchicine	($32 \mu\text{g ml}^{-1}$, 2 days)	4.6 ± 2.1 (11)	
	(Lumicolchicine)	9.1 ± 3.3 (16)	0.51†
Colchicine	($4 \mu\text{g ml}^{-1}$, 3 days)	4.1 ± 1.8 (12)	
	(L-15)	8.7 ± 2.8 (8)	0.47†

Ca spikes were elicited in nerve cells immersed in a Na-free, TEA⁺-rich medium, as seen in Fig. 2. All values are mean $\pm$ s.d.; numbers of sampled nerve cells are indicated in parentheses. Note that there was no significant change in Ca spikes for nerve cells exposed to cytochalasin B. For further details see text.

* $P < 0.02$; † $P < 0.01$ (Student's *t*-test).

related to synaptic vesicles but not to the plasma membrane²⁹. Second, microtubules are easily depolymerized by Ca ions^{4,30} which pass through the Ca channels. Thus, we cannot exclude the possibility that the change in the Ca spikes may be due to wide changes in cellular structure, such as changes in cell shape. Indeed, Ca spikes become large during growth of neurites in tissue culture¹⁵, and are considered to form major action potentials in dendrites of cerebellar Purkinje cells³¹. Thus, the small Ca spikes may be due to a loss of neurites caused by microtubule breakdown after colchicine treatment of the nerve cells.

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Immunochemical and immuno-cytochemical localization of S-100 antigen in normal human skin

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The S-100 antigen¹ is generally considered to be unique to the nervous system, where it is found primarily in the cytoplasm and nucleus of glial cells, both in soluble and bound form^{2,3}. It belongs to the family of acidic Ca²⁺-binding proteins⁴. In phylogenesis, S-100 conserves a close immunological relationship between different species, and during ontogenesis the pattern of its accumulation parallels the functional maturation of the nervous system^{2,3}, although its biological role remains to be clarified. Recently, S-100 has been found in cells of non-nervous organs (interstitial cells of the pineal gland⁵, stellate cells of the adenohypophysis^{6,7} and satellite cells of the adrenal medulla⁸), and in cultured malignant human melanomas⁹. We report here the presence of S-100 in normal human skin, where the antigen seems to be located specifically in melanocytes and in cells with morphological features of Langerhans cells.

Table 1 S-100 protein concentration in normal human skin and malignant human melanoma

Tissue	µg S-100 per mg soluble protein
Normal skin	0.03
Malignant melanoma	1.90

Normal human skin (0.5 g per experiment) and malignant human melanoma (1.0 g per experiment), tested by histopathology, were obtained from the neck and leg during surgery (three specimens each of normal human skin and human melanoma). The tissues were homogenized in a glass homogenizer in 10 mM Tris-HCl, pH 7.4 (1:4 w/v), containing 0.1 mM phenylmethylsulphonylfluoride (Sigma) to minimize proteolytic degradation²¹. The homogenates were centrifuged at 105,000g for 60 min at 4°C and the supernatants analysed for total protein by the method of Lowry *et al.*²², and for S-100 content by microcomplement fixation¹⁰ using as a standard ox S-100 purified as described by Moore¹. Samples with complement alone and with both complement and antiserum were assayed to test the anticomplementary activity of tissue extracts and antiserum. S-100 values are expressed in terms of ox S-100 equivalents. All measurements were performed in duplicate; all values were corrected for anticomplementary activity, when present. The antiserum was diluted 1:500 before the assay. Maximal s.e.m. was ±5% (n = 3). The bound fraction was not evaluated.

Levels of S-100 were measured by microcomplement fixation assay¹⁰, both in normal skin and, for comparison, in human melanomas, using a specific antibody raised against ox S-100 and characterized as described elsewhere¹¹. Cross-reactivity between ox and human S-100 protein has been observed^{11,12}. The complete complement fixation curve for extracts of normal human skin and a standard curve of S-100 protein are shown in Fig. 1a, b. The amounts of S-100 were measured in samples containing 15 or 25 µg total protein (~100–165 µg protein ml⁻¹); no appreciable anticomplementary activity was observed at these concentrations. The S-100 antigen was detected in measurable amounts in both normal skin and melanoma, with an ~80 times higher concentration in the latter than in the former (Table 1). The concentration of S-100 in the skin seemed to be ~100 times lower than that reported for the human brain⁹.

The cellular and subcellular localization of S-100 in normal human skin was also investigated by electron microscopy using the unlabelled antibody PAP method¹³ with the same

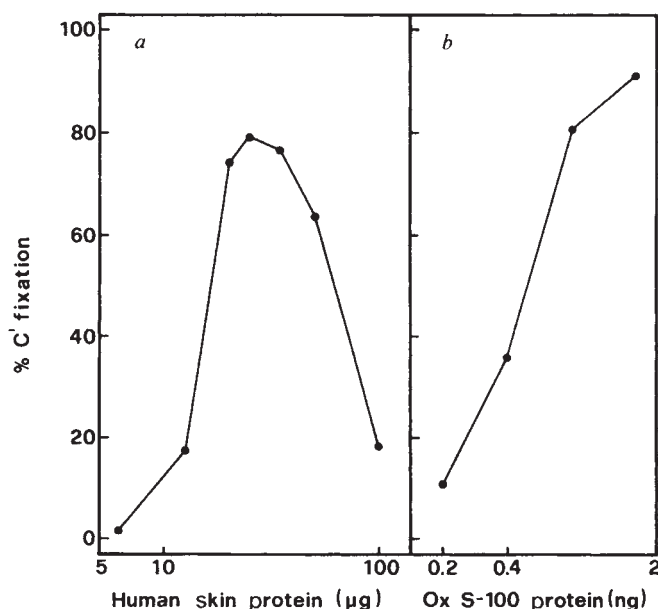


Fig. 1 Representative complement (C') fixation curves of S-100 from normal human skin (a), and of purified ox S-100 (b). Normal skin extract and purified S-100 were prepared, and quantitative complement fixation performed as described in Table 1 legend. All values were corrected for anticomplementary activity, when present.

antiserum. In the epidermis, S-100 reaction product was detected in the perikarya and in the cytoplasmic processes of both melanocytes and Langerhans cells (Fig. 2a, b). No reaction product was present in the keratinocytes of any epidermal layer (Fig. 2a). Merkel cells were not observed in our preparations. In the dermis, S-100 reaction product was detected not only in typical Langerhans cells (which appeared as elongated cells with indented nuclei and slender processes lying close to the other cell types, exhibiting the distinctive cytoplasmic granules; Fig. 2c), but also in cells with ultrastructural features comparable with Langerhans cells but lacking the characteristic granules (Fig. 2d). It is possible that these are Langerhans cells having granules that are not detectable in the plane of the section, or 'histiocytes' or 'dermal macrophages' having the latent capacity to become manifest as dermal Langerhans cells by production of the characteristic granules¹⁴. Fibroblasts and collagen fibres, lymphocytes, vascular endothelial cells and pericytes had no reaction product. Melanocytes and nerve fibres were not detected in the dermis.

The subcellular distribution of the antigen was the same in all the S-100-immunoreactive cells. Immunoreactivity was widely distributed in the cytoplasmic matrix but absent from the cisternae of the endoplasmic reticulum and the Golgi apparatus, as well as from the plasma membranes and mitochondria (Fig. 2a-d). Melanosomes and Langerhans granules also appeared free of reaction product (Fig. 2a-c). In the nucleus, immunoreactivity was found in the nucleoplasm but not in the nucleolus or the nuclear envelope (Fig. 2a, b, d). Control experiments carried out using preimmune rabbit serum or anti-S-100 antiserum absorbed with the antigen did not show any

reaction product (Fig. 3a, b). Thus the distribution of the antigen in immunoreactive cells of the skin seems similar to that reported for S-100-immunoreactive cells of nervous^{15,16} and non-nervous organs⁵⁻⁸.

Our findings agree with recent observations on the presence of S-100 in malignant human melanomas⁹. In addition, they indicate that definite cutaneous cell types normally contain significant amounts of the antigen, but at a much lower concentration than in malignant tissue. No detectable amounts of antigen in normal human skin were reported by Gaynor *et al.*⁹ as tested by microcomplement fixation assay; this discrepancy could be accounted for by use of different titres of antisera. The presence of S-100 in normal melanocytes rules out the possibility of the protein being regarded as a marker unique to malignant melanocytes. In this respect, detailed studies will be needed to establish any possible relationship between levels of S-100 and the degree of malignancy of melanomas, as reported for human tumours of glial origin¹⁷.

The presence of S-100 in melanocytes agrees with the neuroectodermal origin of this cell type^{18,19}. On the other hand, the observation that Langerhans cells contain S-100 is intriguing, as these are generally believed to be mesodermal in origin^{18,20} and data on the cellular localization of S-100 indicate that the protein is present in cells commonly considered to be of neuroectodermal origin^{2,3}. It is also possible that Langerhans cells take up S-100 passively, although the distribution of the antigen both in the cytoplasm and the nucleus, similar to that observed in other S-100-immunoreactive cells^{5-8,15,16}, seems to oppose this view.

Our present data, together with the recent findings of S-100

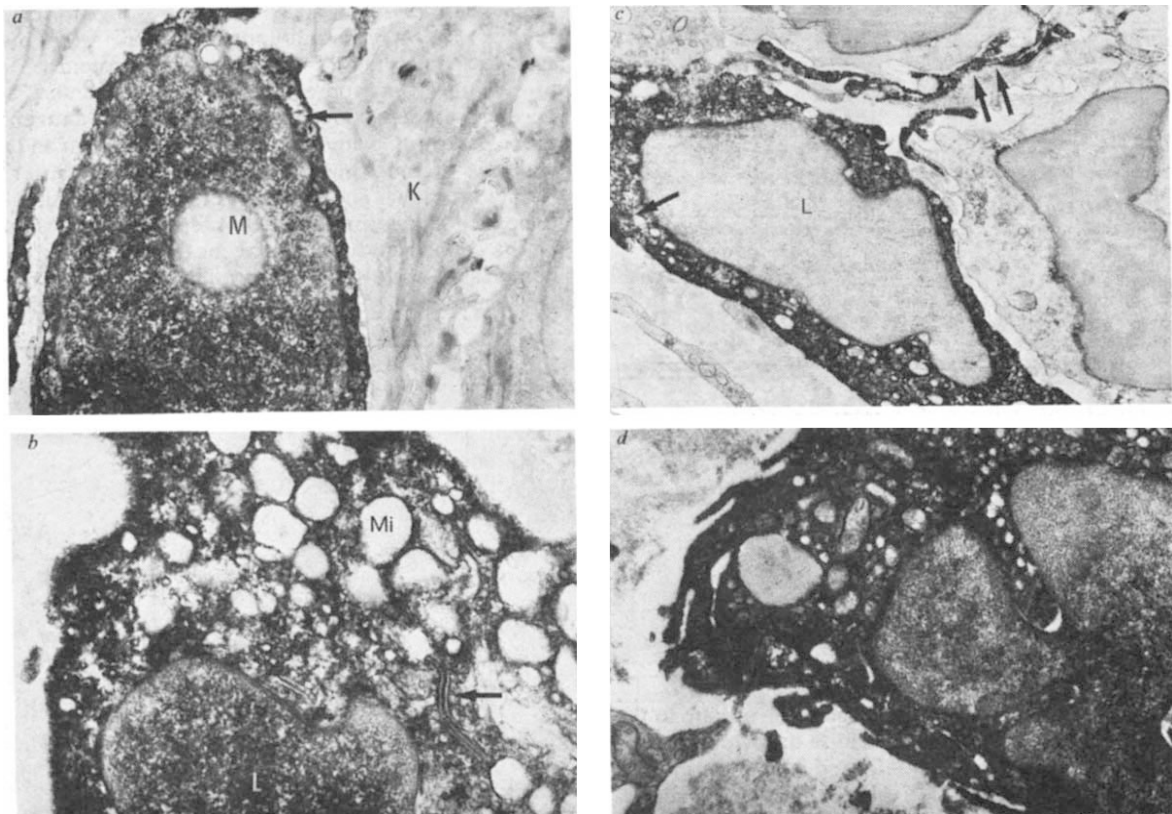


Fig. 2 Sections of normal human skin reacted with anti-S-100 antiserum. Normal human skin obtained from the neck or leg regions during surgery on three patients was fixed in 4% paraformaldehyde in 0.1 M phosphate buffer for 3 h, washed in phosphate-buffered saline (PBS) overnight and then sectioned on a Sorvall TC-2 chopper. The sectioned slices were treated with anti-S-100 antiserum diluted in PBS at 1:500, using the unlabelled antibody PAP method as described elsewhere⁸. *a*, The melanocyte (M) is labelled in the nucleoplasm as well as in the cytoplasmic matrix. No reaction product is present in the nucleolus and in melanosomes (arrow). The keratinocytes (K) do not show any reaction product. *b*, The epidermal Langerhans cell (L) shows immunoreactivity in the nucleoplasm as well as in the cytoplasmic matrix. The mitochondria (Mi) and the typical cytoplasmic organelles (arrow) are free of reaction product. *c*, The dermal Langerhans cell (L) with the distinctive organelles (arrow) shows reaction product in the cytoplasmic matrix. No reaction product is detectable in the nucleus, possibly due to insufficient penetration of antibodies during the immunocytochemical procedure, as also observed elsewhere^{7,8,16}. Labeled Langerhans cytoplasmic processes (double arrow) are closely related to other cell types which seem to lack immunoreactivity. *d*, The dermal Langerhans-like cell shows S-100 immunoreactivity in the nucleoplasm as well as in the cytoplasmic matrix. *a*, $\times 11,400$; *b*, $\times 23,000$; *c*, $\times 11,400$; *d*, $\times 18,300$.

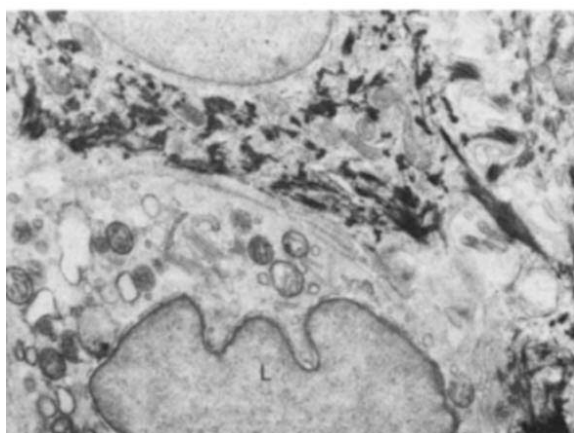
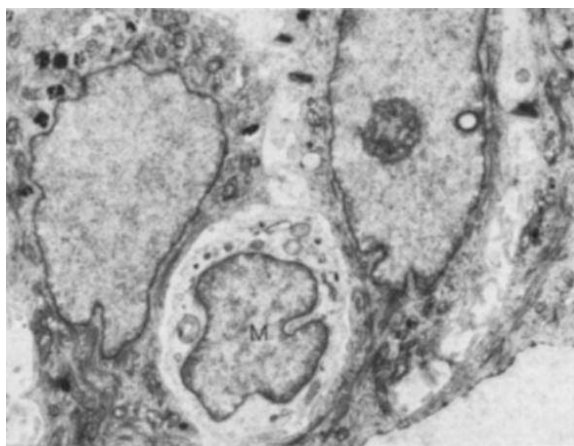


Fig. 3 Control sections of normal human skin treated as described in Fig. 2 legend but reacted with anti-S-100 antiserum absorbed with S-100 antigen. Neither the melanocyte (M) nor the epidermal Langerhans cell (L) show any reaction product. The same results were obtained when sections were treated with normal preimmune rabbit serum. *a*, $\times 9,400$; *b*, $\times 14,300$.

antigen in non-nervous organs in normal conditions⁵⁻⁸, suggest that S-100 should no longer be considered strictly as a protein specific to the nervous system. Further studies on the general tissue distribution of S-100 will be needed to clarify whether the protein is confined to cell types of common embryonic origin.

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Isoleucine-requiring *Nicotiana* plant deficient in threonine deaminase

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Well characterized auxotrophic mutants would greatly assist the genetic manipulation of flowering plants, but such mutants are rare¹⁻³. Moreover, auxotrophic mutants isolated at the plant level⁴⁻⁸ and some of those isolated in cell cultures⁹ are leaky. The isolation of the first non-leaky auxotrophic mutant, requiring a source of nitrogen in reduced form, was possible by direct selection for chlorate resistance of this rare mutant type¹⁰. A different approach, the individual testing of colonies grown from mutagenized haploid cells of *Datura*¹¹ and *Hyoscyamus*¹², has resulted in cell lines with absolute nutritional requirement. We report here the isolation of an isoleucine-requiring line from haploid cell cultures of *Nicotiana plumbaginifolia* and the regeneration of diploid plants. These plants have no detectable activity of L-threonine deaminase (EC 4.2.1.16), the first enzyme in isoleucine biosynthesis.

Haploid protoplasts were prepared from leaves of *N. plumbaginifolia* plants, mutagenized by irradiation and grown to small colonies in complete medium. Calli derived from non-irradiated protoplasts were not studied. Two out of 11,049 colonies tested after mutagenesis were unable to grow on minimal medium (Table 1); they were later identified as a uracil (URA401) and an isoleucine (ILE401)-requiring line by growing them on media supplemented with various amino acids, vitamins and nucleic acid bases following the test system of Holliday¹³. Normal growth of URA401 and ILE401 (Fig. 1) could be restored by feeding 100 mg l⁻¹ uracil and 200 mg l⁻¹ isoleucine, respectively. Characterization of the URA401 line will be reported elsewhere.

Plants could be regenerated only from the ILE401 line. The regenerates were diploid (Fig. 2), although selection was carried out using haploid cells. Diploidy can be explained by spontaneous polyploidization known to occur frequently in cultured plant cells¹⁴. The plants, and the calli initiated from them, have an absolute requirement for isoleucine.

Table 1 The frequency of auxotrophic clones

Dose (J kg ⁻¹)	% Survival	No. (frequency) of clones tested	
			auxotrophs
13	57	3,727	0
16	23	3,705	0
19	15	2,377	0
23	11	1,240	2 (1.6 × 10 ⁻³)

Haploid *N. plumbaginifolia* protoplasts were isolated from sterile plants²¹, irradiated with ⁶⁰Co γ rays²² and cultured in K3 medium²³ supplemented with 0.1% casein hydrolysate and 0.05% yeast extract. The colonies were then individually transferred onto RM medium²⁴ containing 0.1 mg l⁻¹ 1-naphthaleneacetic acid and 1.0 mg l⁻¹ benzyladenine (RMOP medium) and the same supplements as before. Calli (5-10 mm in diameter) were then halved and subcultured onto minimal (casein hydrolysate and yeast extract omitted) and supplemented RMOP medium. Auxotrophs were identified by their inability to grow on minimal medium. Dose rate was 0.042 J per kg per s. % Survival = % of non-irradiated control. Plating efficiency in cultures of non-irradiated protoplasts was ~70%.

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Fig. 1 Nutritional requirement of the ILE401 line. *a*, Minimal RMOP (see Table 1 legend) medium; *b*, minimal medium with 200 mg l⁻¹ L-isoleucine; *c*, minimal medium with 100 mg l⁻¹ α-aminobutyric acid. Cultures were incubated for 3 weeks in the light (2,000 lx, 16 h).

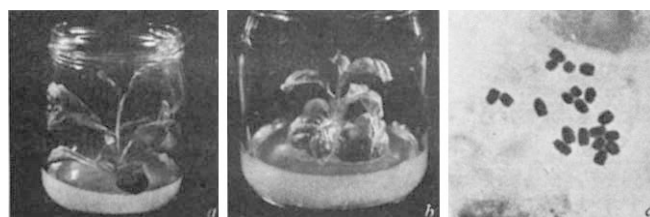


Fig. 2 Wild-type diploid *N. plumbaginifolia* (*a*) and ILE401 (*b*) plants. Metaphase chromosomes in root tips of an ILE401 auxotrophic plant are also shown (*c*).

Except for the first and last steps of their biosynthetic pathway, isoleucine and valine are synthesized by a common set of enzymes in microorganisms¹⁵ and in flowering plants¹⁶. As isoleucine alone is sufficient to restore normal growth of the ILE401 line, it may be defective in either threonine deaminase or transaminase B (Fig. 3). There was no detectable threonine deaminase activity in crude extracts of the ILE401 line, in contrast to the wild type, in which the specific activity was 1.0×10^{-3} μmol per min per mg protein, a value comparable with those found in other plant species^{17,18}. Transaminase B activity, however, was not affected in the mutant. Specific activities in the mutant and wild type were 5.2×10^{-4} and 3.9×10^{-4} μmol per min per mg protein, respectively. (Details of the assays of both enzymes are given in Fig. 3 legend.) The isoleucine requirement of the ILE401 line is therefore due to the absence of threonine deaminase activity. Normal functioning of the rest of the pathway was shown in growth tests in which isoleucine could be substituted with α-aminobutyric acid (Fig. 1), which is converted *in vivo* to α-ketobutyric acid¹⁹, the product of threonine deaminase. To avoid complications due to feedback inhibition by excess isoleucine²⁰, α-aminobutyric acid was used in the test, rather than α-ketobutyric acid, to provide a physiological concentration of α-ketobutyric acid (thus indirectly that of isoleucine).

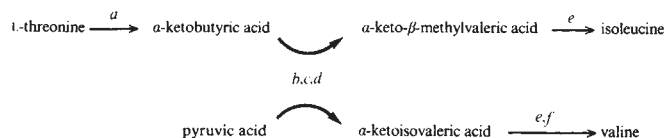


Fig. 3 The isoleucine-valine pathway. *a*, Threonine deaminase; *b*, acetoacetyl acid synthase; *c*, acetoacetyl acid isomeroreductase; *d*, dihydroxy acid dehydrase; *e*, transaminase B; *f*, transaminase C. Extracts for the enzyme assays were prepared by grinding 1 g leaf tissue in 3 ml buffer (50 mM KH₂PO₄, 20 mM 2-mercaptoethanol (2-ME), 2 mM EDTA, pH 8.0) and centrifuging the homogenate at 15,000g for 10 min. Threonine deaminase activity was measured at 37°C in the presence of 62.5 mM KH₂PO₄, 40 mM L-threonine, 5 mM 2-ME, 0.5 mM EDTA, pH 8.0. α-ketobutyric acid formed was determined by the direct method of Friedemann and Haugen²⁵. Transaminase B activity was measured at 37°C in the presence of 30 mM α-ketoglutaric acid, 25 mM L-isoleucine, 12.5 mM KH₂PO₄, 5 mM 2-ME, 0.5 mM EDTA and 0.1 mM pyridoxal phosphate, pH 8.0, using the reverse reaction. α-keto-β-methylvaleric acid formed was determined by the indirect method of Friedemann and Haugen²⁵.

The isoleucine requirement of the ILE401 line may be a result of a mutation or of epigenetic changes³. The low frequency of this phenotype, stability in culture for more than a year and expression at the plant level support the former³. Preliminary data on fusion with recessive mendelian pigment mutants indicate that isoleucine (and uracil) auxotrophies are recessive traits. A detailed genetic analysis of the ILE401 plants is in progress.

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Mouse IgG3 antibodies are highly protective against infection with *Streptococcus pneumoniae*

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Carbohydrate and protein antigens have been shown to elicit the bulk of their antibodies in mutually exclusive IgG subclasses in humans, mice, rats and horses¹⁻⁴. In the mouse, anti-protein antibodies are primarily of the IgG1 subclass, and anti-carbohydrate antibodies are primarily of the IgG3 subclass^{1,2}. We have now demonstrated that mouse IgG3 antibodies to the phosphocholine (PC) determinant of pneumococcal C-carbohydrate^{5,6} and to type 3 pneumococcal polysaccharide are highly protective against experimental type 3 pneumococcal infection. This is the first demonstration that antibodies of the IgG3 subclass can protect against bacterial infection.

Previously we have demonstrated that hybridoma IgM anti-PC antibody can protect mice from infection with type 3 *Streptococcus pneumoniae*⁷ strain WU2. Other data (ref. 8 and J. B. Robbins, personal communication) indicate that hybridoma anti-PC antibody can also protect against pneumococcal types 1, 4 and 6A. Much of the anti-PC antibody produced by inbred mice expresses the variable region idiotype marker, T-15 (ref. 9). Antibodies with this idiotype have virtually identical hyper-variable region sequences¹⁰, affinity for PC¹⁰ and specificity for PC analogues¹¹. We have used protection studies with T-15-

positive hybridoma antibodies of different isotypes¹¹ to compare the effects of differences in constant regions without having to consider differences in specificity.

CBA/J mice were infected intravenously (i.v.) with 10⁶ colony-forming units (CFU) of strain WU2 type 3 *S. pneumoniae*. This dose is 10 times the LD₅₀ (dose that kills 50% of infected mice). Passively administered IgG3 anti-PC antibody was almost 90-fold more protective against *S. pneumoniae* on a weight basis than IgM antibody of the same idiotype (Table 1). Similarly, IgG3 anti-type 3 antibody was almost 40 times more protective than IgM anti-type 3 antibody. Protection was not observed for IgA anti-PC antibody, IgM anti-salmonella antibody, or IgG3 anti-levan antibody. Anti-type 3 antibodies were ~6–15-fold more protective by weight than anti-PC antibodies. This was expected as the PC determinants, which form part of the cell wall⁶, should be largely buried beneath the type-specific capsule¹².

We repeated these studies with (CBA/N×DBA/2)F₁ mice, which express the X-linked immunodeficiency *xid*^{13,14}, make extremely low levels of natural anti-PC antibody^{7,15} and fail to produce anti-type 3 antibody when immunized¹³. These mice were infected with 150 CFU (~10×LD₅₀) of *S. pneumoniae* strain WU2. IgG3 anti-PC antibodies protected *xid* mice ~10 times more effectively than IgM anti-PC antibodies, but IgG3 and IgM antibodies to the type 3 capsule showed roughly equal protective ability (Table 2). As with normal animals, anti-type 3 IgM was more effective than anti-PC IgM antibodies; however, IgG3 antibodies of the two specificities provided similar protection. The reasons for the different relative protective abilities of IgG3, IgM, anti-PC and anti-type 3 antibodies in normal and *xid* mice are unclear, but may be related to differences in immunoresponsive potential and levels of natural serum antibody of the two types of mice, or to the 4-log difference between the infectious doses used in the two studies.

Table 1 Ability of antibodies reactive with pneumococcal cell wall and capsule to protect CBA/J mice against infection with *S. pneumoniae* strain WU2

Hybridoma or myeloma*	Specificity	Idiotype†	Isotype†	PD ₅₀ (µg per injection)‡
59.6C5	PC	T-15	IgG3	0.6
PC-5-2	PC	T-15	IgM	55
T-15 and H-8	PC	T-15	IgA	>300
16.3	SSS-III	?	IgG3	0.1
CA3-1	SSS-III	Unique	IgM	4
CC4-6	SSS-III	Unique	IgA	>200
J606	Levan	J606	IgG3	>200
ST-1	Salmonella typhimurium	?	IgM	>200

Mice were infected i.v. with 10⁶ CFU of *S. pneumoniae*⁷, and protected with intraperitoneal (i.p.) injections of 0.1 ml of the indicated immunoglobulin in doses of 0.02, 0.2, 2.0, 20 or 200 µg (or 100 or 300 µg) 1 h before infection and 1 and 2 days after infection. Injection of diluent alone (0.1% fetal calf serum) was not protective. Antibody and diluent solutions were all filter-sterilized (0.22 µm) before injection. Over 80% of deaths occurred within 4 days of infection. The experiment was discontinued after 10 days.

* Myeloma antibodies T-15, H-8 and J606 and hybridoma protein 59.6C5 were isolated by affinity chromatography^{11,20,25}. Hybridoma proteins 16.3, CA3-1, CC4-6 (ref. 26), ST-1 (ref. 27) and PC-5-2 (a gift from John Kearney) were used as diluted ascites fluids. The amount of antibody in these fluids was quantitated by radioimmunoisotype assays²⁸. Comparable dilutions of normal mouse serum were not protective.

† Determination of the idiotypes and isotypes has been described previously^{9,11,26,28}; ? indicates unknown idiotype.

‡ PD₅₀, dose of passive antibody calculated²⁹ to protect 50% of the mice from fatal infection. At least six to eight mice were tested at each dose.

Table 2 Ability of antibodies reactive with pneumococcal cell wall and capsule to protect (CBA/N×DBA/2)F₁ male mice from *S. pneumoniae* strain WU2

Hybridoma or myeloma	Specificity	Idiotype	Isotype	PD ₅₀ (µg per injection)
59.6C5*	PC	T-15	IgG3	0.6
134.5B11*	PC	T-15	IgG3	0.7
PC-5-2	PC	T-15	IgM	6
22.1A4 ^c	PC	T-15	IgM	4
140.7C6.2*	PC	T-15	IgM	6
T-15 and H-8	PC	T-15	IgA	>300
16.3	SSS-III	?	IgG3	0.6
CA3-1	SSS-III	Unique	IgM	0.8
J606	Levan	J606	IgG3	>100
ST-1	Salmonella typhimurium	?	IgM	>200

The mice used here express the X-linked immunodeficiency (*xid*) defect of CBA/N mice, have no naturally occurring anti-PC antibody^{7,15} and are highly susceptible to pneumococcal infection. Mice were infected i.v. with 100 CFU of *S. pneumoniae* and protected as described in Table 1 legend.

* Anti-PC hybridoma antibodies¹¹ were produced and isolated as described in Table 1 legend.

The more efficient protection by IgG3 antibody in normal and *xid* mice is even more striking considering the fact that divalent IgG3 would be expected to have a much lower avidity than an IgM molecule for identical binding sites. IgM, which is only poorly recognized by Fc receptors^{16–18}, probably acts by opsonizing *S. pneumoniae*, using its highly efficient complement fixation¹⁹. The mechanism of IgG3-mediated killing is not so obvious. Although unaggregated IgG3 does not bind complement C1 (ref. 20), IgG3 anti-streptococcal group A carbohydrate antibody¹ can apparently lyse antigen-coated red blood cells in the presence of complement²¹. Thus the C3b receptor of phagocytes may play a part in IgG3-mediated bactericidal activity. Fc receptors for IgG3 (ref. 22) probably contribute to the anti-pneumococcal protection observed here, as they mediate phagocytosis of sheep red blood cells (SRBC) in the presence of IgG3 anti-SRBC antibody²².

The possibility that IgG3 may mediate bactericidal activity by an antibody-dependent cellular cytotoxicity is suggested by the fact that human natural killer cells can kill bacteria²³, and the recent demonstration that passive IgG3 anti-tumour antibody can protect against tumour growth far better than IgM antibody of the same specificity²⁴.

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The switch region associated with immunoglobulin C_μ genes is DNase I hypersensitive in T lymphocytes

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It is not known whether the antigen-specific receptor of T lymphocytes is encoded by conventional immunoglobulin genes. Several T-cell lines, as well as thymus cells, have been found to contain aberrant IgM mRNAs, but other T-cell lines are apparently negative¹⁻⁴. Rearrangement of *D* and *J* gene segments which code for portions of immunoglobulin heavy (H) chain variable (V) regions has been observed in some T cells, but no complete *V-D-J* rearrangements, as required for *H* gene expression in B cells, have been found⁵. To investigate the chromatin structure around the C_μ gene in T lymphocytes, we have probed the regions flanking the gene by mild digestion with DNase I. We report here that T-lymphocyte chromatin exhibits sites hypersensitive to DNase I in a region 5' of C_μ. In B cells, this region has been proposed to be responsible for switching to downstream C_H genes.

It has been observed in other systems that there are sites in chromatin which are hypersensitive to cleavage by DNase I⁶⁻¹⁰. The location of such sites can be related to the restriction map of a specific gene. It was postulated that the hypersensitivity occurs at DNA sites which may regulate gene activity in the vicinity⁶⁻¹⁰. To determine whether hypersensitive sites are associated with

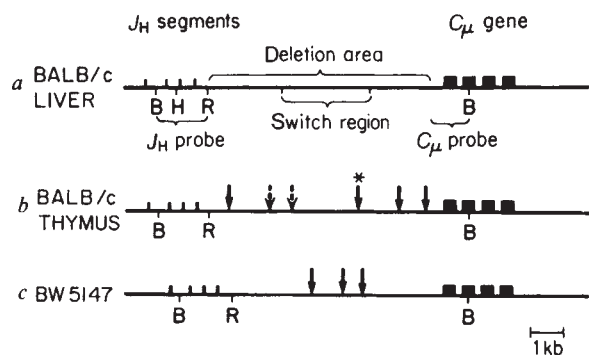


Fig. 1 Restriction maps of the region 5' of the C_μ gene (modified from Liu *et al.*¹⁶). Deletion area¹⁵⁻¹⁷ and switch region¹⁸⁻²² were reported for several plasmacytomas to be involved in the deletion of sequences 5' of C_μ and the switch to other C_H genes, respectively. Vertical arrows indicate DNase I-hypersensitive sites (the stippled arrows indicate sites in thymus visible with the J_H probe, but indistinct with the C_μ probe); *, site that was only visible with the C_μ but not with the J_H probe—this site seems also to be hypersensitive in purified DNA (see Fig. 3). The J_H probe is a *Bam*HI-*Eco*RI fragment cloned by K. Marcu into pBR322 (ref. 15). The C_μ probe is a *Bam*HI-*Eco*RI (artificial *Eco* site) fragment from a germ-line library clone subcloned into pBR322 (R. Near, E. Selsing and U.S., unpublished results).

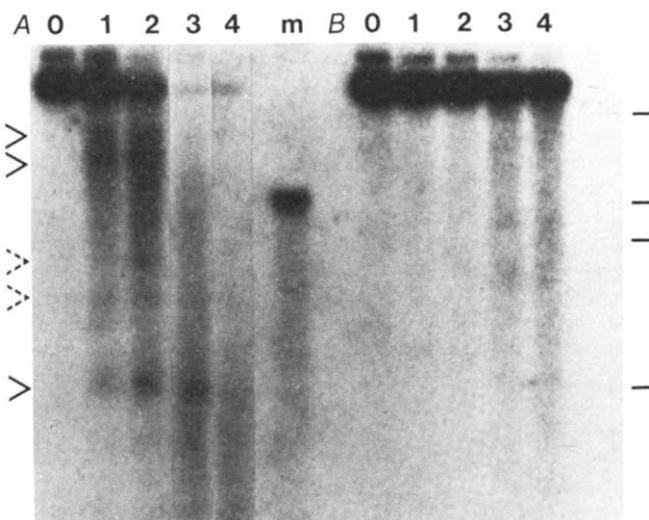


Fig. 2 Southern blots of thymus (A) and liver (B) DNAs from untreated nuclei (track 0) and nuclei treated with DNase I (tracks 1-4) to reduce gradually the size of the DNA to an average of 15-20 kb (track 4)¹². The DNAs were prepared and digested with *Bam*HI¹³. Southern blots²⁸ were produced and hybridized with a J_H probe (see Fig. 1a). Sizing markers are indicated along the right-hand side of the gel—λ phage DNA cut with *Ava*I (8.5, 6.1, 4.8 and 2.2 kb). m, Radiolabelled sizing marker due to the hybridization of the plasmid probe with the 4.6-kb phage λ DNA fragment. Subfragments flanked by a *Bam*HI site and a DNase I-hypersensitive site are indicated by arrowheads. The major hybridization band is the J_H-C_μ gene; the faint fragments above it are due to incomplete digestion by *Bam*HI.

the C_μ gene in T lymphocytes, nuclei from thymus cells (>99% T lymphocytes¹¹) and liver cells (as a control) were prepared and mildly treated with DNase I¹². The range of DNase I concentrations used has been shown to digest active immunoglobulin genes without affecting inactive genes and the bulk of the DNA¹². DNA was extracted from these nuclei and analysed by restriction enzyme digestion together with Southern filter hybridization to map DNase I-hypersensitive sites⁸. A restriction map of the C_μ gene, indicating the enzyme sites used in the analyses, is shown in Fig. 1a.

Liver cells were analysed to provide controls representing a tissue in which immunoglobulin genes are not expressed^{12,13}. When liver DNA, extracted from untreated nuclei, was digested with *Bam*HI and hybridized with a particular J_H probe (see Fig. 1a) a single restriction fragment of 9.8 kilobases (kb) was observed (Fig. 2B, track 0). DNAs extracted from liver nuclei treated with increasing amounts of DNase I showed the same *Bam*HI restriction fragment (Fig. 2B, tracks 1-4). No additional bands were observed, indicating that there are no DNase I-hypersensitive sites in this region of the liver genome.

Thymus DNA, extracted from untreated nuclei, and hybridized with the J_H probe also showed the 9.8-kb *Bam*HI restriction fragment (Fig. 2A, track 0) seen with liver DNA. This supports the conclusion that in most thymus cells no DNA rearrangement has occurred in the region between J_H and the C_μ gene. In contrast to the results obtained with liver cells, however, DNase I treatment of thymus nuclei resulted in the appearance of new fragments (indicated by arrows in Fig. 2A). These subfragments must be flanked by a *Bam*HI site at one end and a DNase I-hypersensitive site at the other. As the J_H probe represents the 5' end of the 9.8-kb J_H-C_μ *Bam*HI fragment (Fig. 1a), the length of the subfragments produced by DNase I digestion indicates the distance between the *Bam*HI site within the J_H cluster and the DNase I-hypersensitive sites (Fig. 1b) thus allowing localization of the hypersensitive sites in the J_H-C_μ map.

We have confirmed the location of DNase I-hypersensitive sites in thymus chromatin by analysis with a C_μ probe (see

Fig. 3 DNase I-hypersensitive sites in pure DNA. Pure thymus DNA was digested with 16 ng ml^{-1} (A) and 32 ng ml^{-1} (B) DNase I for 1 min at 22°C , the reaction was stopped with EDTA, the DNA treated with proteinase K and phenol, and then precipitated with ethanol. The size of the DNAs was determined by electrophoresis in agarose gels and found to be slightly degraded to the same size as DNAs 1 and 2 (Fig. 2A) from DNase I-treated thymus nuclei. The DNAs were treated with *Bam*HI, Southern blots²⁸ prepared and hybridized with the C_μ probe. The arrowhead indicates a subfragment.



Fig. 1a). This probe represents the 3' end of the 9.8-kb J_H - C_μ 1a). This probe represents the 3' end of the 9.8-kb J_H - C_μ *Bam*HI fragment (see Fig. 1a). As before, liver DNA did not show any hypersensitive sites but subfragments were observed for thymus DNA (not shown). The map positions of the major hypersensitive sites in thymus DNA obtained with the C_μ probe coincided with those obtained using the J_H probe. Some subfragments apparent with the J_H probe (stippled arrows in Figs 1b and 2A) were not discrete using the C_μ probe (possibly due to a high background in the C_μ blot).

The hypersensitivity of most of the sites of this genomic area is probably due to the chromatin conformation within thymocyte nuclei. One of the sites, however, may correspond to a nucleotide sequence that is preferentially digested by DNase I, because it is also observed when purified DNA is treated with DNase I (Figs 1 and 3B). It is intriguing that this site is masked in liver chromatin (not shown). The DNA sequence in this region which promotes increased DNase I susceptibility in pure DNA remains to be determined.

The large number of hypersensitive sites observed in thymus chromatin could result from the mixed population of T lymphocytes in the thymus. We have also tested a monoclonal T-cell line, BW5147 (ref. 14), for the presence of DNase I-hypersensitive sites. Mapping of hypersensitive sites in BW5147 is slightly complicated by the fact that in the AKR mouse strain from which this cell line is derived, there is a 0.8-kb deletion between the *Bam* site within C_μ and the *Eco*RI site 5' of the gene (data not shown; see also ref. 15). The deletion is located somewhere within the 'deletion area' marked in Fig. 1a, where deletions in several mouse strains and cell lines have been reported¹⁵⁻¹⁷. There is apparently no rearrangement between the *Bam*HI sites within J_H and C_μ in BW5147, as the *Bam*HI fragments are of the same size in BW5147 and AKR kidney DNA (data not shown). Using the same strategy as described above, three subfragments were observed in DNase I-digested BW5147 DNA for either the C_μ (not shown) or the J_H probe (Fig. 4, tracks 1-4). As with thymus DNA, the hypersensitive sites in BW5147 DNA map 5' of C_μ (Fig. 1c). Obviously there are fewer hypersensitive sites in the DNA of the monoclonal BW5147 cells than in thymus, which may indicate that the complexity of the thymus pattern results from multiple cell populations. We are now exploring this hypothesis further by thymus cell fractionation.

The subfragments produced by DNase I digestion of thymus or BW5147 nuclei are less sharp than restriction fragments; therefore the hypersensitivity is not restricted to a single nucleotide but may span more than 100 base pairs (bp). The same observation has been made for DNase I-hypersensitive

sites associated with immunoglobulin genes in B cells (U.S. and B.A., unpublished data), and with heat-shock genes in *Drosophila*¹⁰. The exact location of the C_μ -associated sites with respect to DNA sequence remains to be determined.

We have not found any hypersensitive sites within 12 kb 3' of the C_μ gene in thymus or liver cells (data not shown). Together with the fact that liver DNA has no hypersensitive sites 5' of the C_μ gene, the defined hypersensitive sites 5' of C_μ in T cells suggest that this area of the genome has been preferentially activated in these cells. This behaviour is analogous to the induced DNase I-hypersensitive sites associated with active globin genes in haematopoietic cells⁹. 'Constitutive' DNase I hypersensitivity of sites in the vicinity of heat-shock genes of *Drosophila*^{8,10} can probably be explained by the fact that these genes have some, albeit low, transcriptional activity at normal temperature¹⁸.

In B cells the central portion of the intron between J_H and C_μ has been postulated to be involved in the switching from expression of C_μ to other C_H genes, because in plasmacytomas which express C_H genes located 3' of C_μ and which have deleted C_μ , a 5' portion of the J_H - C_μ intron was retained¹⁹⁻²³. In different cells different switch sites were used. Further analyses of other B cells may show that switch sites are located throughout the region between J_H and C_μ , as this entire area seems to be prone to deletions¹⁵⁻¹⁷. We have found DNase I-hypersensitive sites in the part of the genome in B lymphocytes that expresses the C_μ gene (U.S. *et al.*, unpublished data). This may reflect the potential of these cells to switch to another C_H gene.

It is intriguing to speculate that the hypersensitive sites in T cells may be involved in the potential of T cells to 'switch' to the expression of a downstream gene—either one of the C_H genes active in B lymphocytes or a T-cell-specific gene. Other explanations for the hypersensitive sites in T cells must also be considered. Normal T cells and some T-cell lines produce C_μ -containing RNAs^{1,2,4}, which probably do not include correctly joined *VDJ* complexes (F. Alt, personal communication). Most of these μ RNAs have their promoter 5' of J_H , but it cannot be ruled out that some are initiated in the switch region (F. Alt, personal communication). Thus, it is unknown whether any or all of the C_μ -associated DNase I-hypersensitive sites of T cells mark transcriptional promoters.

Finally, it is possible that the hypersensitive sites in T cells are not directly correlated with any function. First, they may simply

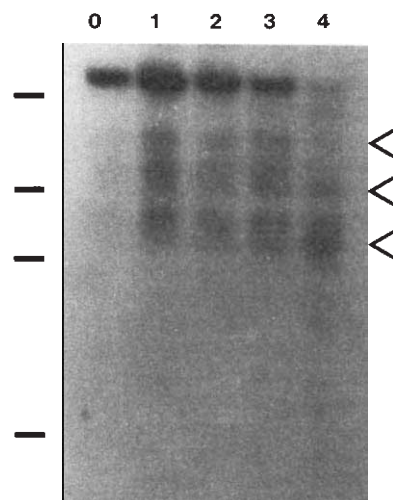


Fig. 4 Southern blot of BW5147 DNA from untreated nuclei (0) and nuclei treated with DNase I (tracks 1-4) to reduce gradually the size of the DNA to an average of 20 kb (ref. 12). *Bam*HI digestion was followed by Southern blotting¹³ and hybridization with J_H probe. Sizing markers indicated along the left-hand margin are λ phage DNA cut with *Ava*I (see Fig. 2 legend). Subfragments flanked by a *Bam*HI site and a DNase I-hypersensitive site are indicated by arrowheads.

reflect the origin of T cells from a lymphoid precursor common to B and T cells. However, in this context it is surprising that B cells show only one hypersensitive site in this region (U.S. and B.A., unpublished results) compared with at least three in T cells. Second, these sites may have become activated in the course of the activation of some other T-cell-specific gene in the vicinity. This would be analogous to the finding of aberrant rearrangements of immunoglobulin genes in B lymphocytes

which express some other functionally rearranged immunoglobulin gene²⁴⁻²⁷. The part which B-cell immunoglobulin genes play in T-cell function remains to be elucidated.

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Introduction of a rabbit β -globin gene into the mouse germ line

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The introduction of cloned foreign genes into cultured mammalian cells¹⁻⁷ has been used to identify DNA sequences required for correct transcription *in vivo*⁸⁻¹⁰. It is not clear, however, to what extent these systems will be useful for an analysis of the sequences necessary for tissue-specific gene expression. A more appropriate approach for such an analysis might be the production of mice that contain a cloned foreign gene in all their cells, throughout development. This could be accomplished by the transfer of a cloned gene into germ-line cells, and the subsequent transmission of that gene to offspring. Previously, SV40 DNA sequences¹¹ and a cloned HSV-1 thymidine kinase gene¹² have been introduced into somatic tissues of mice by microinjection of the DNAs into blastocysts¹¹ or eggs¹², but germ-line transmission of these sequences has not been demonstrated. The only foreign DNA sequences which have been transferred into and transmitted by the mouse germ-line have been exogenous Moloney leukaemia virus genomes introduced by viral infection of early embryos¹³. We now report the introduction of a cloned rabbit DNA fragment containing the adult β -globin gene into the germ-line of mice. We have analysed 24 mice derived from eggs microinjected with this DNA. Nine mice contain the rabbit β -globin gene in liver DNA, and at least four males from this group transmit the gene to a fraction of their progeny.

Fertilized eggs were recovered 3-7 h before first cleavage from (C57BL/6 $\times$ CBA/H)F₁ female mice that had been mated to (C57BL/6 $\times$ CBA/H)F₁ males, and one pronucleus was injected with DNA, using a glass micropipette¹². The DNA was prepared from a recombinant bacteriophage, λ CH4A. β G2 (λ R β G2), which contains the rabbit adult β -globin gene, β 1, and a β -like pseudogene, Ψ β 2, in a 19-kilobase pair (kbp) chromosomal DNA fragment¹⁴⁻¹⁶ (see Fig. 1). Most of the λ R β G2 DNA was in the form of linear monomers but a small fraction (10-20%) consisted of multimers, noncovalently joined by the cohesive ends of λ DNA. Approximately 1 pl of DNA solution, at concentrations ranging from 5 to 50 μ g ml⁻¹, corresponding to 100-1,000 λ R β G2 molecules, was injected into a

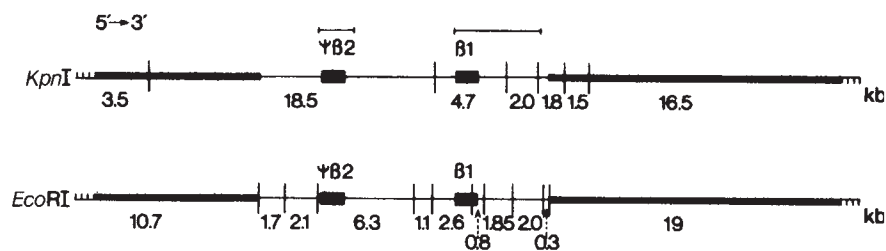
pronucleus. Eggs that survived injection (50%) were transferred to the oviducts of pseudo-pregnant (C57BL/6 $\times$ CBA/H)F₁ females¹⁷, and 15% of them developed to term, yielding a total of 51 live-born mice. Partial hepatectomies were performed on 24 of the mice at 6-8 weeks of age. Total liver DNA was extracted, digested with the restriction endonuclease *Kpn*I and screened for rabbit β -globin sequences by Southern blot hybridization¹⁸.

Figure 2 shows the results for the first 18 mice. Eight of these mice contain sequences in their liver DNA which hybridize to probes for the rabbit β -globin genes, β 1 and Ψ β 2. The most intensely hybridizing bands correspond in size to three λ R β G2 *Kpn*I fragments homologous to the probes (18.5, 4.7 and 2.0 kbp; see Fig. 1). Of six more mice screened (data not shown), one also contains the same λ R β G2 *Kpn*I fragments. The average number of copies of the rabbit β -globin gene per liver cell in each of the positive mice may be estimated from the intensities of hybridization relative to known amounts of *Kpn*I-digested λ R β G2 DNA in parallel lanes. Mice 40 (not shown) and 7 contain 1 or 2 copies, mice 3, 4, 13, 37 and 38, 5-10 copies, and mice 9 and 23, more than 20 copies. Although the sample size is small, there is no obvious correlation between the concentration of the injected DNA and the presence or copy number of λ R β G2 sequences in these mice.

To determine whether the λ R β G2 sequences are transmitted through the male germ line, we mated four male mice containing the rabbit sequences with normal CBA/H females. Total DNA was prepared from several whole newborn progeny, restricted with *Eco*RI and screened for λ R β G2 sequences using ³²P-labelled λ R β G2 DNA as a probe. As shown in Fig. 3, all four mice transmitted λ R β G2 sequences to a fraction of their progeny. These fractions are: one out of four progeny for mice 4 and 23, two out of four for mouse 7, and two out of six for mouse 13. Progeny from the other five positive mice have not yet been analysed. For at least two of the mice transmitting rabbit β -globin sequences (mice 4 and 7), the intensity of hybridization to λ R β G2 is significantly greater for the progeny DNAs than for the parent liver DNAs. One likely explanation is that these mice are chimaeric, and only a fraction of their liver cells contain the λ R β G2 sequences, whereas all the cells of their progeny contain them. If this is so, the apparent number of copies in liver DNA may underestimate the true copy number in those cells that do contain λ R β G2 sequences. A further analysis of the tissue distributions and transmission patterns of the rabbit DNA sequences should distinguish between this and alternative explanations.

The results shown in Fig. 3 also provide information about the structure of the λ R β G2 sequences present in the cells of the

Fig. 1 Restriction maps of $\lambda\text{R}\beta\text{G2}$ DNA. $\lambda\text{R}\beta\text{G2}$ consists of a 19-kbp rabbit chromosomal DNA fragment (thin line) cloned in a bacteriophage λ -vector (thick lines)^{14,24}. βI and ΨB2 (solid boxes) are, respectively, the adult β -globin gene and a β -like pseudogene^{15,16}. The symbols --- and --- represent the single-stranded cohesive ends of the λ vector DNA. DNA was isolated from purified phage particles²⁴ and dissolved in 10 mM Tris pH 7.4, 0.1 mM EDTA for injection into mouse eggs. The bars drawn above the *KpnI* restriction map depict the regions of $\lambda\text{R}\beta\text{G2}$ that are contained in the probes used in Fig. 2.



positive mice and their progeny. Whereas *EcoRI* digestion of linear $\lambda\text{R}\beta\text{G2}$ DNA generates fragments of 19 and 10.7 kbp, corresponding to the two arms of the λCH4A vector (see Fig. 1), the mouse DNAs do not contain the 19- and 10.7-kbp fragments; but in every case, a 30-kb band equal in length to the sum of the two λ vector arms is seen. In addition, all the bands expected from *EcoRI* digestion of the rabbit DNA insert in $\lambda\text{R}\beta\text{G2}$ are detected in the DNAs of the positive mice. Together with the results of Fig. 2, these data suggest that the parent liver and progeny DNAs contain intact copies of $\lambda\text{R}\beta\text{G2}$. The 30-kbp *EcoRI* band in the mouse DNAs is not sensitive to denaturation in conditions that melt the cohesive ends of λ DNA¹⁹ (65 °C, 0.01 M Tris, pH 8), which indicates that the $\lambda\text{R}\beta\text{G2}$ copies exist as either circular or multimeric molecules whose cohesive ends have been covalently joined in the mouse cells.

One possible interpretation of these data is that the $\lambda\text{R}\beta\text{G2}$ sequences are integrated into mouse chromosomes in tandem arrays. In this case, the 30-kbp *EcoRI* fragment in the mouse DNAs would be derived from the joining of the left and right ends of adjacent $\lambda\text{R}\beta\text{G2}$ molecules. Linear DNA molecules are rapidly ligated into high molecular weight concatemers following injection into fertilized frog eggs²⁰, and DNA-mediated transformation of mammalian cells by the calcium phosphate precipitation method is believed to involve the formation of large DNA concatemers before chromosome integration^{21,22}. Possibly, microinjected $\lambda\text{R}\beta\text{G2}$ DNA integrates by a similar mechanism in mouse eggs or early embryos. This interpretation predicts that new *EcoRI* fragments which hybridize to $\lambda\text{R}\beta\text{G2}$ should be generated at the ends of each integrated array of $\lambda\text{R}\beta\text{G2}$ molecules. Most of the positive mouse DNAs do, in fact, show one or more new, fainter *EcoRI* bands in addition to the strong bands that are due to multiple copies of $\lambda\text{R}\beta\text{G2}$. These are visible in several of the lanes of Fig. 3. Mouse 13, for example, shows a new *EcoRI* fragment about 12 kbp in length (panel e, lane B) which is inherited by both of its positive progeny (panel d, lanes B and F). Mice 7 and 23 (panels b and c) also show new *EcoRI* fragments which are transmitted to their progeny. The observation that these new bands are inherited is consistent with the prediction that the bands represent junction fragments generated at sites of chromosomal integration. As no more than two or three new bands are seen in either *KpnI* or *EcoRI* digests of the positive DNAs, it is unlikely that the mice could contain many individually integrated copies of $\lambda\text{R}\beta\text{G2}$. Although our data support a model of chromosomal integration, they do not formally eliminate other interpretations, such as the autonomous replication and germ-line transmission of free $\lambda\text{R}\beta\text{G2}$ circles. We are now attempting to detect integration of the rabbit DNA sequences by *in situ* hybridization to metaphase chromosomes²².

In conclusion, we have demonstrated that a large eukaryotic DNA fragment can be introduced at a high frequency into mouse tissues, in the absence of selection, and transmitted through the germ line. Therefore, many strains of mice can now be produced that carry the adult rabbit β -globin gene and its flanking sequences in all their cells. With such strains of mice it will be possible to examine the expression of the rabbit β -globin gene and to investigate whether expression is restricted to specific tissues and/or developmental stages. If the rabbit sequences are integrated into mouse chromosomes, presumably different strains will contain the rabbit genes at different

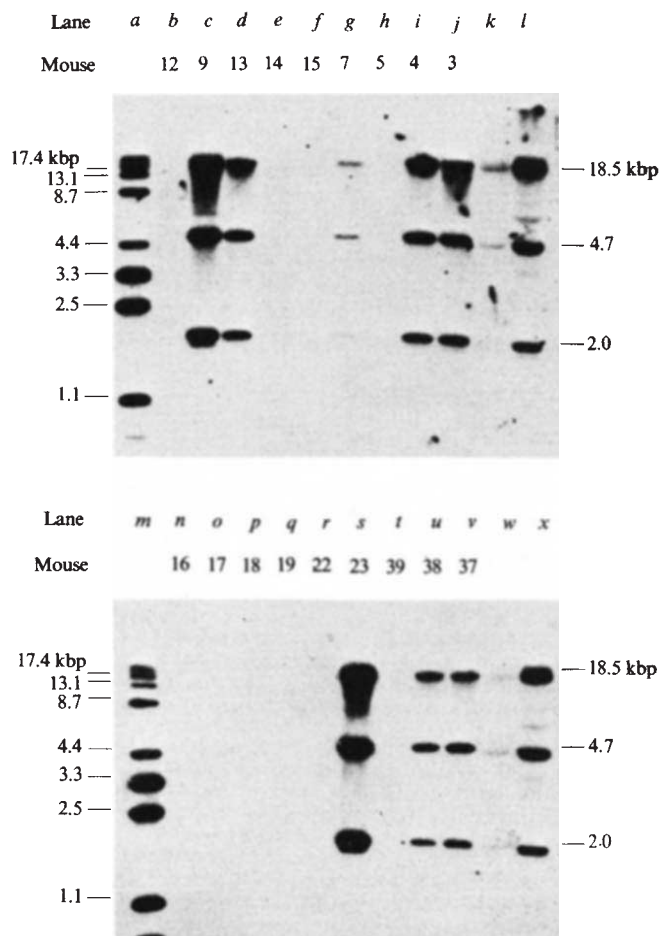


Fig. 2 Detection of $\lambda\text{R}\beta\text{G2}$ sequences in mouse liver DNAs. Liver tissue samples (0.2–0.4 g) were surgically removed from 6–8-week-old mice, frozen in liquid nitrogen and stored at -80°C . High molecular weight DNA was extracted by the method of Blin and Stafford²⁵ with the following modifications. Powdered frozen tissue was suspended by pipetting in 0.1 M EDTA, 0.05 M Tris pH 8 and subsequently brought to 0.5 M NaCl, 0.5% (v/v) Sarkosyl and 250 $\mu\text{g ml}^{-1}$ proteinase K. Before the final dialysis step, the DNA was precipitated with ethanol. Yields ranged from 200 to 800 μg of DNA from each liver sample. 10 μg of each DNA was digested with *KpnI* (New England Biolabs), fractionated by electrophoresis on 0.75% agarose gels and transferred to nitrocellulose filters¹⁸ following cleavage by partial depurination²⁶. The hybridization probe was a mixture of two plasmids, one containing the βI gene on a 5.6-kbp *PstI* fragment and the other containing the ΨB2 gene on a 2.3-kbp *EcoRI*–*BglII* fragment. The regions of $\lambda\text{R}\beta\text{G2}$ corresponding to these probes are shown in Fig. 1. Probe DNA was labelled with ^{32}P by nick translation²⁷ to a specific activity of 4×10^8 d.p.m. per μg and used at a concentration of 7 ng ml^{-1} . Filters were prehybridized for 6 h and hybridized for 18 h essentially as described by Wahl *et al.*²⁶. After hybridization the filters were washed for 12 h at 66°C in $2 \times \text{SSC}$, 0.5% SDS, 0.01 M sodium phosphate pH 6.8, 0.05% sodium pyrophosphate and 0.001 M EDTA, and then for 1 h at 55°C in a 10-fold dilution of the same buffer. In these conditions, no cross-hybridization between the rabbit β -globin probe and normal mouse DNA is detected. Lanes a and m, molecular weight markers. Lanes b–j and n–v, *KpnI*-digested liver DNA from 18 mice derived from injected eggs. Lanes k and w, 80 μg of *KpnI*-digested $\lambda\text{R}\beta\text{G2}$ DNA plus 10 μg of salmon sperm DNA. Lanes l and x, 800 μg of *KpnI*-digested $\lambda\text{R}\beta\text{G2}$ DNA plus 10 μg of salmon sperm DNA. These amounts correspond to 1 and 10 copies of $\lambda\text{R}\beta\text{G2}$ per diploid genome in 10 μg of mouse DNA, and the limit of detection on the autoradiographs was 0.1–0.2 copies per diploid genome. The 18.5-, 4.7- and 2.0-kbp fragments of $\lambda\text{R}\beta\text{G2}$ hybridize strongly to the probe whereas the 1.8-kbp fragment hybridizes weakly. Other bands visible in the digest of $\lambda\text{R}\beta\text{G2}$ (lanes l and x) are partial digestion products.

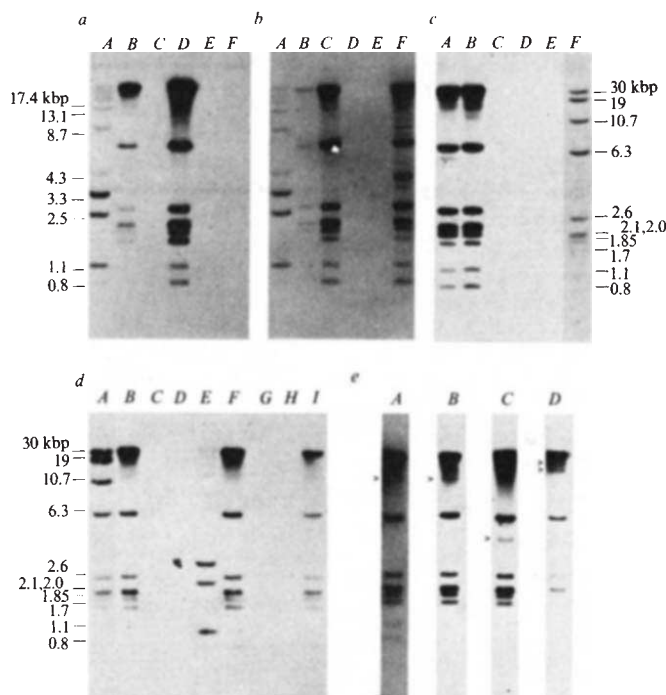


Fig. 3 Transmission of λ RBG2 sequences through the male germ line. Four male mice containing λ RBG2 sequences in liver DNA were mated to normal CBA/H females and total DNA was isolated from their whole newborn progeny. Liver DNAs from the four males (10 μ g) and total DNAs from their progeny (10 μ g) were digested with *Eco*RI (Boehringer), fractionated on 0.5% agarose gels and blotted. Filters were hybridized to 32 P-labelled λ RBG2 DNA (2.4×10^8 d.p.m. per μ g; 10 ng ml $^{-1}$). Panel a: lane A, molecular weight markers whose sizes are indicated on the left; lane B, liver DNA from mouse 4; lanes C–F, total DNAs from four progeny of mouse 4. Panel b: lane A, molecular weight markers; lane B, liver DNA from mouse 7; lanes C–F, total DNAs from four progeny of mouse 7. The DNA sample in lane F is incompletely digested by *Eco*RI. Panel c: lane A, liver DNA from mouse 23; lanes B–E, total DNAs from four progeny of mouse 23; lane F, a mixture of linear monomers and concatemers of λ RBG2 digested with *Eco*RI. The 19- and 10.7 kbp fragments are the λ vector arms of monomeric linear λ RBG2 (see Fig. 1). The 30-kbp fragment derives from concatemers and consists of the 19- and 10.7-kbp fragments joined by the λ cohesive ends. The smaller fragments are the *Eco*RI digestion products of the rabbit DNA insert in λ RBG2. Panel d: lane A, same as lane F of panel c; lanes B–D and F–H, total DNAs from six progeny of mouse 13; lane E, molecular weight markers; lane I, liver DNA from mouse 13. Panel e: *Eco*RI-digested liver DNAs from four of the positive mice hybridized to 32 P-labelled λ RBG2 DNA. Each lane is exposed to show one or more new, faint bands not characteristic of λ RBG2. Lane A (a longer exposure of lane I, panel d) contains liver DNA from mouse 13 and shows a faint band at ~12 kbp, which is also visible in two of the progeny of mouse 13 (lanes B and F, panel d). Lane B contains liver DNA from mouse 7 and shows a faint band of ~13 kbp, which is visible in at least one of the progeny of mouse 7 (lane C, panel b). Lane C contains liver DNA from mouse 37 which shows a new band at ~4.5 kbp. Lane D contains liver DNA from mouse 38 which shows two new bands at roughly 15 and 20 kbp. Progeny from mice 37 and 38 have not been analysed.

chromosomal locations. This will allow us to investigate how the host chromosomal environment influences the expression of a foreign gene²³.

Since the submission of our manuscript, chromosomal integration of the λ RBG2 sequences in mouse 23 has been demonstrated by *in situ* hybridization to metaphase chromosome spreads prepared from peripheral blood. The probe was 125 I-labelled λ RBG2 DNA, and hybridization was performed as described by Robins *et al.*²². In every metaphase spread examined (19), intense labelling was observed at a site in the middle of one homologue of chromosome 1. This indicates that most if not all of the copies of λ RBG2 in this mouse are integrated into chromosome 1.

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Transcriptional regulation of the prolactin gene by ergocryptine and cyclic AMP

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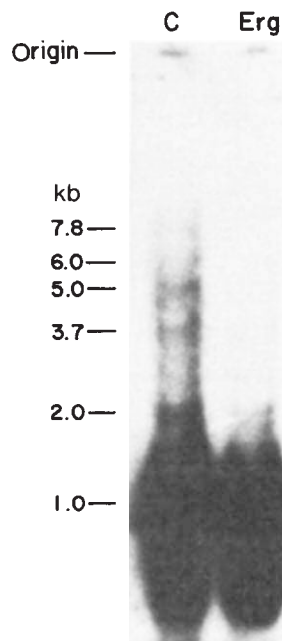
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A large body of evidence suggests that the synthesis^{1,2} and secretion^{3–7} of the pituitary hormone prolactin is inhibited by the hypothalamic hormone dopamine. The finding that dopamine inhibits adenylate cyclase activity of rat pituitary⁸ and human prolactin-secreting adenoma⁹ suggests that the dopaminergic inhibition of prolactin synthesis may be mediated by decreased levels of cyclic AMP. Recently, the dopaminergic inhibition of prolactin synthesis has been shown to involve decreased concentrations of prolactin mRNA^{2,10}. Furthermore, monobutyl cyclic AMP increases prolactin mRNA levels in pituitary cells treated with the potent dopaminergic agonist ergocryptine¹¹. Such changes in prolactin mRNA levels could involve transcriptional or post-transcriptional events. Here we report that treatment of pituitary cells with ergocryptine leads to rapid inhibition of prolactin gene transcription and that addition of monobutyl cyclic AMP to ergocryptine-pretreated cells results in a rapid stimulation of prolactin gene transcription.

We first examined the effect of ergocryptine on the levels of nuclear precursors of prolactin mRNA. Previous work has demonstrated the presence of large, potential precursors of prolactin mRNA in pituitary cell nuclei¹², the largest of these being 7.0 kilobases (kb); the mature prolactin mRNA is 1.0 kb.

Fig. 1 The effect of ergocryptine on possible nuclear precursors of prolactin mRNA. Dispersed pituitary cells were prepared, initially plated in serum-containing medium and then maintained in serum-free Dulbecco's modified Eagle's medium as described previously², except that the cells were plated in large, 15-cm diameter tissue culture dishes. After 2 days in serum-free medium, half the cultures were treated with 10 nM ergocryptine (Erg) while the controls (C) received only saline. After 24 h, the cells were scraped from the plate in phosphate-buffered saline (PBS) and collected by low-speed centrifugation. The cell pellet was homogenized in 0.25 M sucrose, 20 mM Tris pH 7.9, 5 mM MgCl₂, 0.1% Triton X-100 using 12 strokes of the tight pestle of a Dounce homogenizer and 2.0 ml of the homogenate were then layered over a sucrose cushion consisting of 1.5 ml of 0.5 M sucrose, 20 mM Tris pH 7.9, 5 mM MgCl₂ and 1.0 ml of 0.3 M sucrose in the same buffer. The sample was then centrifuged at 1,000g for 10 min. The solution above the sucrose cushion was aspirated, the sides of the tube washed with water and the remaining solution decanted.

The nuclear pellet was resuspended in homogenization buffer and centrifuged through sucrose cushions once more. The nuclear pellet was then dissolved in 7 M guanidine HCl, 20 mM Tris pH 7.4, 1 mM EDTA, 1% Sarkosyl using a Dounce homogenizer. The homogenate was layered over 1.5 ml of 5.7 M CsCl, 0.1 M EDTA and centrifuged at 33,000 r.p.m. at 20 °C for 16 h in the SW50.1 rotor. The RNA which pelleted through the CsCl cushion was dissolved in sterile water and precipitated by addition of 0.1 volume 3 M sodium acetate pH 7 and 2.5 volumes of ethanol. Nuclear RNA (8.8 µg) from control and ergocryptine-treated cells was denatured by treatment with glyoxal and electrophoresed on a 1.25% agarose gel. The RNA was then transferred to nitrocellulose by blotting as described elsewhere²⁷. Prehybridization and hybridization conditions were as described elsewhere²⁷. The hybridization probe was a recombinant DNA plasmid, pPRL-2, labelled with ³²P by nick translation¹⁵ to a specific activity of 2 × 10⁸ c.p.m. per µg. After hybridization the filter was washed as described elsewhere²⁷ then exposed to X-ray film in the presence of an intensifying screen. Numbers indicate the sizes of the RNA species in kb.



Hoffman *et al.*¹³ have recently detected even larger possible precursors of prolactin mRNA. If the dopaminergic inhibition of prolactin mRNA levels involves effects on the transcription of the prolactin gene, then the concentration of the prolactin mRNA nuclear precursors should decrease. Thus we determined the effect of ergocryptine on prolactin mRNA precursors using techniques similar to those used previously¹². Nuclear RNA isolated from ergocryptine-treated and control pituitary cells was denatured with glyoxal, electrophoresed on an agarose gel, then transferred to nitrocellulose. To identify prolactin mRNA species, the filter-immobilized RNA was hybridized to a radiolabelled recombinant DNA plasmid containing the complete prolactin coding sequence¹⁴. This plasmid, pPRL-2, was labelled *in vitro* with ³²P by nick translation¹⁵. Using this procedure, multiple, large RNA species containing prolactin sequences were detected in nuclear RNA from control cells (Fig. 1). In ergocryptine-treated cells, there was a considerable decrease in the hybridization of labelled pPRL-2 to all the high-molecular weight species of prolactin mRNA, which suggests that ergocryptine greatly reduced the concentration of prolactin mRNA precursors in these cells. These results suggest that ergocryptine may inhibit transcription of the prolactin gene. However, the RNA transfer technique has at least two limitations for analysis of gene regulation: (1) it is difficult to obtain quantitative information from the procedure—partly due to the fact that different transfers may have different efficiencies and the RNA bands may be better resolved in some transfers than others; (2) the technique only provides information on the concentration of various prolactin mRNA species; it does not rigorously demonstrate changes in synthesis. Therefore, further experiments were performed in which the *de novo* synthesis of prolactin mRNA sequences was quantitated.

Isolated nuclei provide a useful system for the analysis of transcriptional regulation. In most nuclei transcription systems, RNA synthesis is due primarily to elongation of RNA chains with very little initiation of new RNA chain synthesis^{16,17}. Therefore, when nuclei are allowed to continue RNA synthesis *in vitro*, the RNA produced should accurately reflect RNA

Table 1 Analysis of prolactin mRNA synthesis in isolated nuclei

Nuclei	α -amanitin	Input RNA (c.p.m. $\times 10^{-6}$)	Prolactin mRNA added (μ g)	c.p.m. RNA hybridized		Prolactin cRNA hybridized (%)	Prolactin mRNA synthesis (%)
				pRL-1	pBR322		
Expt 1							
Pituitary	—	1.45	0	444	58	48	0.055
Pituitary	+	0.91	0	65	35	47	0.007
HTC cells	—	3.30	0	60	57	40	0.000
Expt 2							
Pituitary	—	2.10	0	278	69	28	
Pituitary	—	2.10	0.05	210	65	17	
Pituitary	—	2.10	0.1	137	64	8.8	
Pituitary	—	2.10	0.5	94	63	4.1	

Nuclei were isolated from the pituitaries of female, retired breeder rats or from cultured HTC cells as described in Fig. 1 legend. Isolated nuclei were resuspended in 20 mM Tris pH 7.9, 5 mM MgCl₂, 40% glycerol and stored at -70 °C. For transcription, 40 µl of the nuclear suspension were incubated in a 100-µl reaction mixture containing 16% glycerol, 20 mM Tris pH 7.9, 5 mM MgCl₂, 150 mM KCl, 0.4 mM of ATP, GTP and CTP and 250 µCi of [α -³²P]UTP (300–400 Ci mmol⁻¹) at 26 °C for 45 min. Then 50 µg of reticulocyte RNA and 0.4 ml of 10 mM Tris pH 7.4, 5 mM EDTA, 1% SDS, 0.1 mg ml⁻¹ proteinase K were added and the sample incubated at 45 °C for 30 min. RNA was isolated by pelleting through CsCl using a modification of the procedure described in Fig. 1 legend. The proteinase K-digested sample was combined with 2.0 ml of 7 M guanidine HCl, 20 mM Tris pH 7.4, 1 mM EDTA, 1% Sarkosyl and the sample incubated at 60 °C for several minutes until the chromatin dissolved. The sample was layered over 1.5 ml of 5.7 M CsCl, 0.1 M EDTA, then overlaid with mineral oil and centrifuged at 33,000 r.p.m. at 20 °C for 16 h in the SW50.1 rotor. After centrifugation the solution above the CsCl cushion was removed, the sides of the tube rinsed with sterile water and the remaining CsCl solution decanted. The RNA pellet was then dissolved in 0.5 ml water and 2.0 ml of the guanidine HCl-Sarkosyl buffer added and the RNA pelleted through a second CsCl cushion by centrifugation in the SW50.1 rotor as described above. After the second centrifugation the RNA pellet was dissolved in sterile water and precipitated by addition of 0.1 volume 3 M sodium acetate pH 7.0 and 2.5 volumes of ethanol. Transcripts containing prolactin sequences were quantified by hybridization to nitrocellulose disks containing immobilized pPRL-1 DNA. DNA (2 µg) was immobilized on 6-mm nitrocellulose disks as described by Kafatos *et al.*²⁴. Hybridization mixtures of 60 µl contained 0.6 M NaCl, 10 mM HEPES pH 7.4, 1 mM EDTA, 0.2% SDS, 0.1 mg ml⁻¹ yeast tRNA, 800 c.p.m. of prolactin ³H-cRNA, and two filters containing immobilized pBR322 DNA and pPRL-1 DNA. Prolactin ³H-cRNA was included to determine the efficiency of hybridization and was synthesized as described elsewhere²⁵ using prolactin cDNA²⁶ as template. Competitor prolactin mRNA prepared as described²⁶ was added to some of the hybridization mixtures (expt 2). The hybridizations were overlaid with mineral oil and incubated at 68 °C for 36 h. Filters were washed twice with 2 × SSC (SSC = 0.15 M NaCl, 0.015 M sodium citrate) for 30 min each at room temperature, once with 6 × SSC, 0.1% SDS for 30 min at 68 °C, once with 2 × SSC, 0.1% SDS for 30 min at 68 °C, twice with 2 × SSC for 30 min each at room temperature, digested for 1 h at 37 °C in 2 × SSC containing 10 µg ml⁻¹ pancreatic RNase and 1 µg ml⁻¹ T1 RNase, then washed twice with 2 × SSC, 0.1% SDS for 30 min each at room temperature. Radioactivity was eluted from the filters and counted as described by McKnight and Palmiter²⁵. Prolactin mRNA synthesis is expressed as a percentage of total RNA synthesis and was corrected to 100% hybridization of the added prolactin cRNA standard.

Table 2 Effects of ergocryptine and monobutyl cyclic AMP treatment of cultured pituitary cells on prolactin mRNA synthesis by isolated nuclei

Cell treatment	Incorporated UTP (pmol per μ g DNA)	Input RNA (c.p.m. $\times 10^{-6}$)	c.p.m. RNA hybridized		Prolactin cRNA hybridized (%)	Prolactin mRNA synthesis (%)
			pPRL-1	pBR322		
Expt 1						
	Controls	0.024	1,135	106	51	0.042
		0.037	1,481	148	50	0.038
	Ergocryptine	0.032	246	119	47	0.004
Expt 2		0.036	255	92	46	0.005
	Controls	0.030	795	55	36	0.040
		0.029	717	77	33	0.041
	Ergocryptine	0.033	278	64	40	0.009
		0.029	221	50	36	0.009
	Ergocryptine + Bt-cAMP	0.045	783	65	30	0.032
		0.042	703	81	34	0.025

Monolayer cultures of dispersed pituitary cells were prepared, plated in serum containing medium and then maintained in serum-free Dulbecco's modified Eagle's medium as described in Fig. 1 legend. Cells were treated with 10 nM ergocryptine, 10 nM ergocryptine + 0.5 mM monobutyl cyclic AMP (Bt-cAMP), or saline (controls) for 24 h then the cells were scraped from the plate in PBS and collected by centrifugation at 500g for 10 min. Isolated nuclei were prepared from the cells as described in Fig. 1 legend, used to synthesize 32 P-RNA, and prolactin mRNA synthesis determined as described in Table 1 legend.

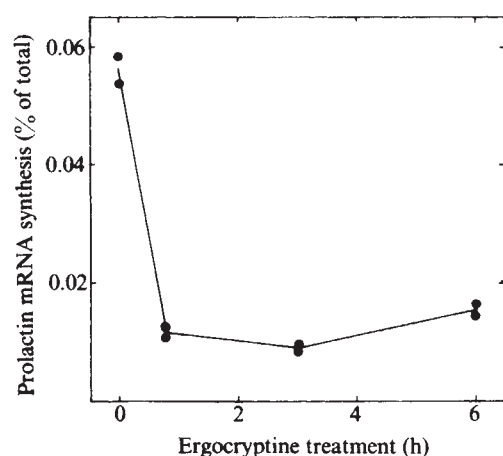


Fig. 2 Time course of ergocryptine effects on prolactin mRNA synthesis. Dispersed pituitary cells from female rats were cultured as described in Fig. 1 legend. After 2 days in serum-free medium, the cells were treated for the time indicated with 10 nM ergocryptine, then scraped from the plates and nuclei prepared. The isolated nuclei were allowed to synthesize RNA and prolactin mRNA synthesis was determined as in Table 1 legend. 32 P-RNA input into each hybridization was $7-10 \times 10^6$ c.p.m. Points indicate values obtained from duplicate independent assays from the same experiment; the line connects average values.

isolated nuclei is tissue-specific, asymmetric and mediated by RNA polymerase II.

Treatment of pituitary cells with ergocryptine for 24 h decreased the synthesis of prolactin mRNA sequences by isolated nuclei (Table 2). In one experiment prolactin gene transcription was reduced nearly 10-fold and in a second experiment there was a >4-fold reduction in prolactin mRNA synthesis. Analysis of the time course of the effects of ergocryptine demonstrated that the inhibition of prolactin gene transcription was rapid (Fig. 2). After 45 min of ergocryptine treatment, the earliest time point examined, prolactin mRNA synthesis was reduced almost fivefold and no greater reduction was detected after 3 or 6 h of treatment.

Simultaneous addition of 0.5 mM monobutyl cyclic AMP partially blocked the ability of ergocryptine to inhibit transcription of the prolactin gene (Table 2). Previous studies have shown that cyclic AMP derivatives have little or no effect by themselves, but that they effectively reverse the dopaminergic inhibition of prolactin synthesis and hence prolactin mRNA levels¹¹. Therefore, the effect of monobutyl cyclic AMP was tested only in cells treated with ergocryptine rather than testing the effect of the cyclic AMP derivative alone. Analysis of the

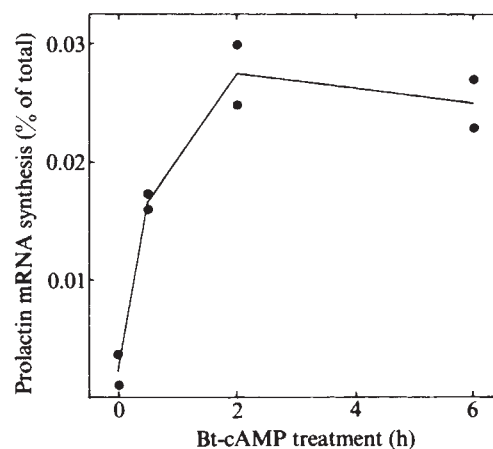


Fig. 3 Time course of monobutyl cyclic AMP effects on prolactin mRNA synthesis in ergocryptine-pretreated cells. Cultured pituitary cells were prepared as in Fig. 1 legend and after 2 days in serum-free medium they were treated with 10 nM ergocryptine for 24 h. Then 1.0 mM monobutyl cyclic AMP (Bt-cAMP) was added for the time indicated (the 0 time point received no cyclic AMP) and nuclei prepared from the cells. Transcription and analysis of prolactin mRNA synthesis were as described in Table 1 legend. 32 P-RNA input into each hybridization was $6-8 \times 10^6$ c.p.m. Points indicate values obtained from duplicate determinations; the line connects average values.

synthesis which occurred *in vivo*. The synthesis of a particular RNA can then be determined by hybridization of the RNA to filter-immobilized recombinant DNA containing the sequence of interest. Nonspecific hybridization was determined using filters containing the wild-type plasmid DNA and this value was subtracted from the radioactivity hybridized to filters containing prolactin recombinant DNA. The rate of prolactin mRNA synthesis was calculated by dividing the radioactivity in specific prolactin sequences by the input radioactivity. This procedure was used to examine prolactin mRNA synthesis in pituitary cell and HTC rat hepatoma cell nuclei (Table 1). Prolactin mRNA synthesis was reduced to near background levels by a concentration of α -amanitin ($1 \mu\text{g ml}^{-1}$) which should inhibit RNA polymerase II (refs 18, 19). Total RNA synthesis was inhibited ~40% by this concentration of α -amanitin. There was no detectable synthesis of prolactin mRNA sequences in nuclei from the HTC cell line. Addition of competitor prolactin mRNA to the hybridization mixture resulted in similar reductions in the hybridization of 32 P-RNA transcripts and prolactin ^3H -cRNA. This demonstrates that the labelled prolactin transcripts result from asymmetric transcription of the sense strand of the prolactin gene. Thus, the synthesis of prolactin mRNA sequences by

time course of monobutyl cyclic AMP effects in ergocryptine-pretreated cells revealed a rapid stimulation of prolactin gene transcription (Fig. 3). After 30 min, prolactin mRNA synthesis was stimulated about eightfold. Apparently maximal stimulation of >10-fold increases in prolactin gene transcription were detected after 2 and 6 h of cyclic AMP treatment.

The time course and magnitude of ergocryptine effects suggest that the principal mechanism involved in the dopaminergic inhibition of prolactin mRNA accumulation is the inhibition of prolactin gene transcription. Ergocryptine induced a 4- to 10-fold reduction in prolactin gene transcription, which is similar in magnitude to its effects on prolactin synthesis and prolactin mRNA levels². This inhibition of prolactin transcription is rapid and clearly precedes the changes in prolactin mRNA levels, which decrease much more slowly².

It seems likely that the dopaminergic regulation of prolactin gene transcription is mediated by cyclic AMP. Previous studies have shown that dopamine agonists inhibit pituitary adenylate cyclase^{8,9}, decrease pituitary cyclic AMP levels^{11,20,21} and inhibit prolactin synthesis and mRNA accumulation^{2,10}. Furthermore, cyclic AMP stimulates prolactin synthesis and prolactin mRNA accumulation in ergocryptine-treated cells¹¹. These studies suggest that in the absence of dopamine, pituitary cells contain high levels of cyclic AMP which stimulate prolactin mRNA accumulation. Thus, dopaminergic treatment decreases cyclic AMP levels, leading to decreases in prolactin mRNA concentrations. The finding that addition of monobutyl cyclic AMP to ergocryptine-treated cells results in a rapid stimulation of prolactin mRNA synthesis demonstrates that the ability of cyclic AMP to alter prolactin mRNA levels involves effects at the transcriptional level.

Recently, cyclic AMP has been shown to alter the transcription of a gene for a developmentally regulated protein of *Dictyostelium discoideum*²². The finding that cyclic AMP affects transcription of the prolactin gene demonstrates that it can also affect gene transcription in higher eukaryotes. This is particularly interesting in view of the effects of cyclic AMP on prokaryotes in regulating the transcription of specific genes²³. In *Escherichia coli*, a cyclic AMP binding protein interacts with specific promoter sites to alter gene transcription. The dopaminergic regulation of prolactin gene transcription may provide a useful model system for further analysis of the role of cyclic AMP in regulating the transcription of eukaryotic genes.

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Effects of dexamethasone and cortisone with X-ray irradiation on transformation of C3H 10T $\frac{1}{2}$ cells

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Hormones can influence carcinogenesis in experimental animals¹ and it has been proposed that sex hormones may act like tumour-promoting agents in their ability to enhance the incidence of cancer². On the other hand, it has been observed that the glucocorticoid hormone, dexamethasone, suppresses the enhancement of chemical carcinogenesis *in vivo*² and of transformation *in vitro*³ brought about by exposure to the tumour-promoting agent, 12-*O*-tetradecanoyl-phorbol-13-acetate (TPA). We report here that the glucocorticoid hormones, cortisone and dexamethasone, do not suppress radiation transformation of C3H 10T $\frac{1}{2}$ cells *in vitro*. Indeed, cortisone induces transformation of cells by itself, and increases the yield of radiation-induced transformants in a synergistic fashion.

We used a cell line^{4,5} derived from C3H mouse embryos (10T $\frac{1}{2}$, clone 8) adapted for studies of radiation transformation⁶⁻⁹. For the transformation assays, cells were exposed to either 0 or 400 rad of X rays, with or without 10⁻⁷ M dexamethasone or cortisone (determined in separate experiments to be the highest non-toxic dose). Dexamethasone or cortisone (Sigma) was added to the cultures immediately after irradiation and subsequently added at each medium change for the entire 6-8-week transformation assay.

The assay has been described in detail elsewhere⁶ and involves identifying and scoring dense foci of cells in a culture dish. Briefly, type 1 foci represent areas of abnormally dense growth, but with no other deviations from normal cell morphology; cells from these foci are not tumorigenic in mice⁶. Type 2 foci are large and the cells are extensively piled up and moderately stellate in appearance⁶; type 2 cells are tumorigenic in 60-75% of inoculated mice⁶. Type 3 foci are large and contain cells that are very densely piled up and which are highly stellate and show marked criss-crossing and swirling at the border of the focus. Type 3 cells are tumorigenic in 80-100% of inoculated mice⁶. Types 2 and 3 foci were scored as transformants, but tabulated separately.

The results (Table 1) show that cortisone (10⁻⁷ M) by itself is capable of inducing transformation in C3H 10T $\frac{1}{2}$ cells, whereas dexamethasone (10⁻⁷ M) is not. When cortisone treatment followed X-ray exposure, the yield of transformants was significantly higher than expected for either agent alone or for the expected additive effect of both agents (using χ^2 analysis with Yates' continuity correction). Thus, for cells exposed to both cortisone and X rays, there seems to be a synergistic response for the induction of malignant transformation. When radiation exposure was combined with dexamethasone treatment, there was also a higher observed yield of transformants

Table 1 Effect of cortisone (10^{-7} M) and dexamethasone (10^{-7} M) on transformation of C3H $10T\frac{1}{2}$ cells

Group	Treatment	Plating efficiency $\bar{x} \pm \text{s.e.}$	Total cells in total no. of dishes	Total no. of observed foci		Fraction of dishes used which contained transformants	
				Type 3	Types 2 and 3	Type 3	Types 2 and 3*
a	Controls (no treatment)	30.9 ± 6.5	12,640	0	0	0/40 = 0	0/40 = 0
b	X-ray irradiation (400 rad)	6.8 ± 1.9	29,038	13	35	12/77 = 0.16	26/77 = 0.34
c	Cortisone alone	31.1 ± 6.7	25,270	18	26	11/78 = 0.14	16/78 = 0.21
d	Dexamethasone alone	21.8 ± 5.7	35,182	1	3	1/78 = 0.01	3/78 = 0.04
e	X-ray irradiation (400 rad) + cortisone	6.0 ± 1.9	26,070	91	116	41/76 = 0.54	54/76 = 0.71
f	X-ray irradiation (400 rad) + dexamethasone	6.8 ± 2.2	32,449	39	60	23/75 = 0.31	34/75 = 0.45

Details of experimental techniques used in radiation transformation experiments on $10T\frac{1}{2}$ cells have been described elsewhere⁶⁻⁹. Stock cultures were maintained in 60-mm Petri dishes and were passaged by subculturing at a 1:20 dilution every 7 days. The cells used were in passages 9-14. These were grown in a humidified 5% CO_2 atmosphere at 37 °C in Eagle's basal medium supplemented with 10% heat-inactivated fetal calf serum and antibiotics. Cells were irradiated 24 h after seeding. Plating efficiencies were determined from three plates seeded with a cell density one-fifth that of the plates used for the transformation assay; these cultures were terminated at 10 days. The various toxicities were considered in the design of the experiments. All dishes used for the transformation assay contained ~300 viable cells per dish. Types 2 and 3 foci were scored as transformants, as described by Terzaghi and Little⁶. We have not quantitated our results in terms of 'transformation frequency per surviving cell' because this method should not be used for the malignant transformation of C3H $10T\frac{1}{2}$ cells, as described in detail elsewhere^{8,9}.

* Chi-square analysis (with Yates' continuity correction) of the data for the fraction of dishes used which contained types 2 and 3 foci gave the following results: group a against b, $P < 0.001$; a against c, $P < 0.01$; c against e, $P < 0.001$; b against e, $P < 0.001$; b against f, $P > 0.05$; b + c against e, $P < 0.05$; b + d against f, $P > 0.05$. In addition, $P > 0.05$ was obtained for the data from the three treatment groups when the fraction of dishes containing only type 3 foci was compared. Fisher's exact test (types 2 and 3 foci): a against d, $P > 0.05$.

than expected for an additive effect of the treatments. However, the yield of transformants after X-ray irradiation and dexamethasone treatment was not significantly greater than the yield of transformants observed for radiation alone or for the expected additive effect of the combined treatments. As similar results were obtained in four separate experiments, these data were pooled (see Table 1).

Mondal and Heidelberger³ reported that dexamethasone suppressed TPA-enhanced transformation *in vitro*, and similar results have been reported for TPA-enhanced chemical carcinogenesis *in vivo*². However, our results indicate that these glucocorticoid hormones do not suppress *in vitro* malignant transformation that has been induced by X rays alone. These results suggest that promotion *in vivo*² or *in vitro*^{9,10} that occurs in the presence of TPA is different from the natural expression of carcinogenesis *in vivo* or transformation *in vitro* effected by exposure to a high dose of a carcinogen such as X-ray irradiation. A similar conclusion was reached in other experiments involving the suppressive effects of several protease inhibitors on X-ray transformation with or without enhancement by TPA^{11,12}. Scribner and Süss¹³ have recently reviewed other evidence for the non-equivalence of complete carcinogenesis, brought about by exposure to a high dose of a carcinogen, and the initiation-promotion carcinogenesis regimen, brought about by a low dose of carcinogen followed by TPA promotion. Cortisone, in that it induced transformation by itself and significantly increased the yield of transformants expected for radiation treatment alone, was similar to 17β -oestradiol in its actions on C3H $10T\frac{1}{2}$ cells¹⁴.

Previous quantitative observations on radiation transformation of $10T\frac{1}{2}$ cells agree with published data on radiation carcinogenesis in experimental animals, in terms of dose-response relationships and the effects of factors such as dose rate, linear energy transfer and modifying agents (for review, see ref. 9). These results suggest that the response of $10T\frac{1}{2}$ cells may be related to the induction of cancer in animals, which is thought to be closely related to carcinogenesis in humans (for review see ref. 15). Thus we believe that our results may have implications for patients treated with a combination of glucocorticoids and cytotoxic agents. For example, patients undergoing total nodal

radiation and combination chemotherapy (which includes glucocorticoid treatment) for Hodgkin's disease have an elevated incidence of secondary leukaemia and lymphoma¹⁶⁻¹⁸. This has commonly been thought to be caused by exposure to combinations of X rays, alkylating agents and procarbazine; our results also implicate glucocorticoids. In addition, patients who are undergoing chronic immunosuppression by glucocorticoids (organ transplant patients) also have an elevated incidence of malignancy¹⁹. Thus, malignancy in transplant patients may be due not only to immunosuppression itself but also to the agents used to achieve this status. Our results lead us to speculate that when the clinical efficacy of glucocorticoids is similar, dexamethasone may give a decreased risk of tumour formation compared with cortisone.

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